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CLINICAL USE OF DIGITALIS IN CONGESTIVE HEART FAILURE *

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INTRODUCTION

The basic defect in congestive heart failure is almost universally conceded to be a loss of power of the heart as a pump, which loss of power is related to a diminished efficiency of contraction of the myocardial fibers. The digitalis drugs are the only substances which are known markedly to increase the contractile power of the heart. It is logical, therefore, that digitalis should be, as it in fact is, the foremost modality of treatment of heart failure.

The active principles of these drugs are composed of three moieties:

1. A prosthetic group which is a ring structure, incorporating an oxygen atom, and characterized by a carbon - carbon double bond, and a carbonyl group in the delta position. This structure, which is an unsaturated lactone, is specific in its inotropic effect, and alterations of the features mentioned markedly diminish the cardiotonic value of the digitalis body to which it is attached.[1] Many biologic substances, including for example, ascorbic acid possess this structure.

2. A cyclopentenophenanthrene nucleus. This is a steroid structure common, with variations, to the adrenocortical and gonadal hormones, and to cholesterol. Its role is as a carrier for the prosthetic group, and probably has to do with specificity of the site of action of the lactone group; the latter has cardiotonic activity of itself but vastly greater when attached to the steroid nucleus. The nucleus has no intrinsic cardiotonic activity; however, variations of its substituents, usually hydroxyls or aldehydes, modify the intensity of the effects of digitalis. The lactone ring is attached to the steroid nucleus at the C-17 position, and the group together is referred to as an aglycone.

3. One or more sugar molecules are attached as a side chain to the steroid nucleus at the C-3 position. This whole molecule is called a glycoside. The number and types of sugars and acetylation or lack of it of the terminal sugar determine the solubility and the duration of effect of the compound, but are not essential to cardiotonic activity.

Clinical effects of digitalis on the heart and circulation in congestive heart failure. Administration of the drug to the subject in heart failure produces the following principal effects:[2-5]

Slowing of the ventricular rate; in sinus rhythm, this is a consequence of compensation; in the presence of auricular fibrillation, this is due to a direct effect on junctional tissue conduction resulting in

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increased atrioventricular block: with small doses, the block is due to vagal effect of digitalis, an effect which is abolished by atropine. There is increased force of systolic contraction, with more complete emptying and increased cardiac output. The duration of systole is shortened, there is increased ventricular filling, and a longer resting period. The diastolic volume is reduced; there is, therefore, a shorter initial diastolic fiber length, hence diminished oxygen consumption per unit work: which is to say there is increased efficiency of the myocardium. The arterio-venous oxygen difference falls, the venous pressure falls, and the pulmonary artery diastolic pressure falls. There is an associated marked diuresis of water, sodium, and chlorides, and a diminution of edema.

Digitalis produces characteristic changes in the electrocardiogram.[6] These include especially a sagging of the terminal portion of the S-T segment, lowering or inversion of T-waves, and shortening of the Q-T interval. These changes are not quantitatively correlatable with the degree of digitalization, and can only give evidence of the presence of digitalis. Their absence does not rule out prior administration of digitalis.

Repeated attempts through the years to prove a site of action of digitalis in areas other than the heart have left few marks to stand against the truly enormous literature concerning the well established myocardial effects of significant magnitude.[7-9] There is recurrent interest in the possible direct renal effect of digitalis, and it does seem that under experimental conditions digitalis may have a direct renal effect; however, the magnitude of such effects is not nearly of the same order as those demonstrated for the myocardium. Inasmuch as digitalis affects several enzyme systems which are widespread in the body,[5, 10] it is not unlikely that changes in a great many discrete functions could be demonstrated, especially with toxic doses of the material.

As to the absorption, fate, and the excretion of digitalis, much remains to be learned. Most of the work in this area has been carried out with digitoxin, and since this drug is unusual in that it is adsorbed on serum albumin,[11] it is not certain that data from its study will apply generally. It is known that digitoxin is removed from the blood very rapidly, and that very little is held in the extracellular fluid;[12] yet it is denied that it has any special affinity for the heart and that it is fixed by this organ.[14] It is a question whether this last is true regarding other digitalis glycosides, and whether it is true in vivo. Certainly, from the clinical viewpoint one loads the body with digitalis, then merely replaces from day to day the daily loss, a situation which strongly suggests a depot exists in the body. Since the heart is the undoubted site of action of digitalis, there is a natural suspicion that it may constitute this depot.

Studies on urinary excretion now possible with isotopically tagged glycosides are as yet fragmentary.[14, 15] It would appear that excretion is proportional to the total amount in the body at a given time, and is variable from subject to subject and from day to day, and that the cardiac excretes it as efficiently as the normal.

MODE OF ACTION

The mode of action of digitalis still defies precise description. However, much reasonable speculation, based on a considerable body of experimental data is available.

Within the myocardial cells energy is delivered to the contractile machine in the form of high-energy phosphate bonds produced by the chain of reactions through which carbohydrate is degraded. This potential energy is housed in the adenosine-polyphosphate - phosphocreatine stores of muscle. The contractile elements themselves are actin and myosin [16] which can exist separately, in an extended form, held apart by ionic forces in which potassium plays a prime role, the structure stabilized by energy supplied by the ATP, and made possible by the semipermeable

nature of the cell membranes, which, while stable, do not allow the passage of charged particles such as potassium ions.[17] This state of pent up potential, which is in electrical equilibrium, constitutes the polarized, resting, presystolic state of the myocardium. The arrival of the impulse from the pacemaker involves the production of acetylcholine which disrupts the equilibrium of the membrane, permits potassium to migrate, breaking the intrafibral ionic equilibrium, permitting actin and myosin to complex, and to assume the least-strained intramolecular arrangement, by spiralling, which perforce results in shorter molecules, hence, shorter fibers, which constitute by their collective shortenings, the contraction of the heart. Now cholinesterase[5] is present to limit the action of acetylcholine; adenosinetriphosphatase,[5] and adenosinetriphosphate-deaminase[5] to deactivate the ATP; and myokinase[10] to inhibit ATPase; and no doubt many other enzyme systems, each with its own relationship to concentration of calcium,[17] magnesium, and other ions. It has been demonstrated that digitalis glycosides are capable of inhibiting[5, 10] or accelerating several of the enzymes mentioned under various conditions, and could therefore favorably influence the gradients of the ADP-ATP-PC system, and the duration of effect and concentration of ACH. Such changes could favor the efficient reconstruction of the structure of potential energy above described. These speculations are not nullified by Wollenberger's finding of unaltered ATP in heart failure,[1] and in any case Proctor has challenged the validity of this finding.[5]

It has also been suggested by Szent Georgyi[16] that digitalis directly affects membrane permeability, and that it may replace some unknown substance normally present, or a substance to which the heart has become refractory. In this connection it is impossible to escape noting the similarity of digitalis to steroid hormones, as well as the fact that certain adrenal steroids produce syndromes which simulate some aspects of heart failure. Considering the numerous examples of biological antagonism[18] encountered in enzyme studies, there might well be such an "unknown substance." The discovery of new adrenal steroids is a recurrent phenomenon, and it is not impossible that some cortical principle involved in congestive heart failure might eventually be found. Of current interest in this area is the report by Titus, Weiss, and Hadju[19] of the isolation of a cardiac active compound from beef adrenal medulla, which they have identified as palmitoyl lysolecithin. The authors mention the work of Klunk and Debuch who identified a substance of this structure in heart muscle. It must be noted that the material in question is a choline compound, which raises a question as to whether the cardiac effect noted might not be an acetylcholine type of effect rather than a digitalis-like effect.

I shall not attempt to list all the available digitalis preparations, but rather those which are in common use and those which are of current interest.

Digitalis leaf, or the whole powdered dry leaf of Digitalis purpurea, is the long standing choice. It contains variable amounts of cardioactive principles and must be standardized biologically. About 20 per cent absorption takes place from the gastrointestinal tract. Its onset of effect is of the order of eight hours, and the duration of effect is one to three weeks. It has the advantages that gastrointestinal symptoms of toxicity occur early, and as a rule before serious cardiac toxic manifestations. Its prolonged effect permits a smoother maintenance with daily doses once this dose has been determined. Also it is relatively cheap. It is remarkable how many patients can be well maintained on a dose of one and a half grains per day. It has the disadvantages that gastric intolerance is not infrequent, and that when toxicity has developed its duration is prolonged to as much as a week or longer. The advent of pure glycosides, which can be standardized by weight, has seriously challenged the popularity of the older prep-

aration. Its chief use is in slow digitalization; for this a prescription of one tablet of a grain and a half, three times daily until signs of digitalization or early toxicity occur is a good method; this will take five to eight days. Digitalis leaf can no longer be considered a useful form for rapid oral digitalization, and has no place at all in parenteral therapy.

Digitoxin, an early example of purified glycoside, is widely used. It is absorbed completely on oral administration so that the oral and parenteral doses are the same. It has a long latent period orally and parenterally, evidently because, as has been shown, it is adsorbed on serum albumin;[11] for the same reason its rate of dissipation is extremely slow. Its onset and its duration of effect are quite similar to these factors for the leaf. It has the advantage of precise oral absorption, and of facility of transfer to parenteral maintenance when the oral route is not available. It has the disadvantages that gastrointestinal warning symptoms of overdosage are often absent; because of its slow onset of effect it is not a drug of choice for rapid digitalization; and, finally, the great duration of effect makes overdosage unusually hazardous. It is not a drug that I use. The digitalizing dose ranges from 1.0 to 1.5 mg, with an average of 1.2 mg. The daily maintenance dose is from 0.1 to 0.2 mg., but toxicity has occurred even at the lower dosage level, and may develop after several weeks on such doses.

Digoxin, not to be confused with digitoxin, is a glycoside of Digitalis lanata. It may be classed as a rapidly acting agent. Its absorption from oral administration is only moderately good, about 70 per cent, so that the parenteral dose is somewhat less than the oral dose. The onset of significant effect on parenteral use is of the order of thirty minutes, and the peak effect about three hours. On oral use the peak effect occurs in about eight hours, and significant effect of a single oral dose is still present at eighteen hours; its elimination is complete or near complete in three days. It can be seen on the one hand that cumulation is involved in the maintenance dosage, and, on the other that effects of overdosage are of short duration. Parenteral digitalization can be accomplished by the intravenous or intramuscular routes using the same solution which is available containing 0.25 mg. per cc. Total digitalizing dose ranges from 1.0 mg. to 1.5 mg. Initially 0.5 mg. may be given, followed by additional 0.25 mg. doses at four to six hour intervals. Oral digitalization may be carried out by giving similar amounts at similar intervals, but is apt to require at least 1.5 mg. as the total dose. Maintenance parenterally is usually 0.25 mg. per day. Oral maintenance requires as a rule 0.375 mg. (that is one and a half of the 0.25 mg. tablets), but quite often 0.25 mg. is an adequate daily dose.

Lanatoside C (cedilanid), a glycoside of Digitalis lanata, differs from digoxin in that it possesses in its sugar moiety an additional glucose, and is acetylated. It also differs in that its absorption from the oral route is extremely poor. Otherwise its characteristics and use closely parallel those of digoxin. It is an excellent agent for rapid parenteral digitalization; it is used intravenously in doses totalling 1.2 mg. to 1.6 mg. While the total amount may be given in one dose in extreme situations, it is better to give perhaps three-fourths of the dose initially, then add further doses if needed to achieve the desired degree of digitalization. Maintenance is possible with an average dose of 0.2 mg. intravenously, per day if necessary, but not very practical. Oral use of this drug is unsatisfactory.

Desacetyl-lanatoside C is a relatively new product derived from lanatoside C by removal of the acetyl group from the sugar moiety. It is said to be more soluble and more stable than the parent drug, and is replacing Cedilanid on the market. The new compound bears the trade name Cedilanid-D. It does not differ materially from the older drug.

Acetyl-digitoxin is another relatively recent innovation. As its name indicates it is closely related to digitoxin, but retains the acetyl group present in the parent glycoside (either purpurea glycoside A or lanatoside A). It is well or completely absorbed orally. Its latent period, peak effect, and persistence are intermediate between digoxin and digitoxin. It remains to be determined whether this drug offers any advantages over existing compounds.

Gitalin, amorphous, is a mixture of glycosides obtained from Digitalis purpurea. It has been used in Europe for some time but has been introduced here only in recent years. Its characteristics are intermediate between digoxin and digitoxin. This drug is of special current interest because it has been stated, especially by Batterman,[20] that its therapeutic dose is less than half the toxic dose. Since in other digitalis preparations the therapeutic dose is at least two thirds of the toxic dose, gitalin would seem to offer a very great advantage in digitalis therapy. However, most pharmacologists believe that toxicity is merely an extension of therapeutic effect in digitalis. A recent report of a comparative study of gitalin and digitalis leaf, by Bryfogle, et al,[21] indicates that in any given case, a decreased toxicity of one preparation was accompanied by a decreased potency, and an increased potency by an increased toxicity. It was found in this study that whereas 0.5 mg. of gitalin demonstrated a therapeutic potency similar to that of 0.1 gm. of digitalis leaf, a decreased toxicity or wider therapeutic range for gitalin could not be demonstrated.

Ouabain, a glycoside of Strophanthus-G, is an extremely potent cardiotonic agent. In doses of 0.25 mg. intravenously a significant degree of digitalization can be produced in less than five minutes. Since toxicity and efficacy go hand in hand the dangers of this drug are obvious. Nevertheless its clinical use may on rare occasions be justified, although possibly as a matter of desperation. Other agents have been mentioned for rapid digitalization which are almost as quick and a great deal safer.

Acetyl strophanthidin is an acetylated aglycone derived from Strophanthus kombé glycosides. Its molecule therefore contains no sugar side-chain. Intravenous administration produces the most rapid and the briefest cardiotonic effect of all. It has been used in the performance of a digitalis tolerance test by Lown and Levine.[4] It would seem to have chiefly experimental interest at this time.

In summary, then, there are a number of effective cardiotonic drugs available, each of which has certain special features. However they all have in common a strengthening effect on the myocardium; they all slow the ventricular rate in auricular fibrillation; and they all have toxic potentialities commensurate with their therapeutic properties. While there may be one ideal agent forthcoming, to date no single drug holds a manifest advantage over all others in all respects. It still is desirable to follow the standard advice to select one agent for routine use and one for rapid digitalization, and to become thoroughly at home with them. In my personal practice I find that digoxin serves quite well for routine and rapid use.

The question naturally arises as to when a patient is adequately digitalized. This is a clinical judgment. He is digitalized when the symptoms of heart failure are subsiding: when breathing is easier, rales are clearing, a gallop rhythm is corrected, the heart rate is tending toward normal: when good diuresis begins, and the patient looks better. In the presence of atrial fibrillation with initially high ventricular rate, digitalization can be recognized by a ventricular rate slowed to sixty or sixty-five, which does not speed up with exercise or with atropinization. When in doubt, doubling the maintenance dose for a few days until very early signs of toxicity are produced should settle the matter. When, in an emergency, the problem arises as to whether the signs present, especially where arrhythmias are involved,

are due to over-digitalization or not, one might resort to the digitalis tolerance test of Lown and Levine. This consists of giving small doses (0.15 to 0.3 mg.) of acetyl strophanthidin intravenously, at five to ten minute intervals, with continuous electrocardiographic observation, to the point of a therapeutic effect or a toxic effect. Potassium is given initially when toxic arrythmia is strongly suspected; and procaine amide is used to control immediately any toxic effect provoked by the test.

Indications for digitalis. The presence of congestive heart failure is sufficient indication for the administration of digitalis. In heart failure associated with acute myocardial infarction digitalis should seldom be resorted to at once; oxygen, morphine and atropine may restore compensation in a few hours. If it is used, it should be done slowly and cautiously, in submaximal doses, and preliminary quinidinization or concomitant use of procaine amide should be considered. Angina pectoris is not a contraindication to digitalis when heart failure is present: compensation should improve coronary flow and may alleviate the angina.[22] Digitalis is of distinct value though not the prime treatment in the heart failure associated with renal insufficiency, toxemia of pregnancy and cor pulmonale; it is of less value in thyrotoxicosis with failure, and of little or no value in heart failure due to anemia, and that due to myxedema. It should be remembered that the common etiological factors for heart failure frequently coexist with some of the more questionable indications for digitalis; in these situations the additional diagnosis should be recognized and the failure attributable to it treated accordingly. In rheumatic fever with failure, as with other types of carditis, digitalis is of limited value, and may be dangerous; however, in selected cases its cautious use may be rewarding. In the presence of complete A-V block, congestive failure is again an indication for digitalis. In partial A-V block [23] there is a relative contraindication; the possibility of completing the block must be weighed against the clear and present danger of uncompensated heart failure; moreover, it is possible that restoration of cardiac efficiency may, by improving coronary flow, actually produce a net result beneficial to the conduction in junctional tissue. Here also atropine might protect conduction to some extent.

Digitalis Intoxication. Toxicity is inherent in the drug. When a therapeutic effect has been obtained it is known that 60 to 70 per cent of the toxic dose has been given. When bigeminy occurs as the result of digitalis it can be assumed that 50 to 80 per cent of the lethal dose has been given. Toxic reactions are increasingly frequent, apparently because of the increasing numbers of older patients with severer heart disease resulting from longer preservation of life in an aging population; also because of treatment methods which commonly lead to depletion of body electrolytes; in addition it is thought by many that the purified glycosides by avoiding early gastrointestinal symptoms fail to give the warning once provided by the whole leaf preparations. Since many of the symptoms of toxicity are simulated by the heart disease itself as well as by intercurrent illness, it is well to assess carefully the symptomatology beforehand so as not to be misled later.

There is a close relationship between the total body potassium and the effects of digitalis. Depleted potassium stores markedly increases the myocardial sensitivity to digitalis; and in animals at least hyperkalemia increases digitalis tolerance. Potassium deficiency is common in congestive heart failure as the result of anorexia, malnutrition, acidosis, low salt diets, mercurial diuretics, Diamox, resins, ammonium chloride, cortisone; also it occurs in certain cases of renal insufficiency and can readily be produced by hemodialysis technics.[24]

The symptoms are many and varied; they are chiefly gastrointestinal, nervous, and cardiac. The first group ranges from nausea to diarrhea. Among the nervous

manifestations, changes in the higher faculties ranging from lassitude to acute psychosis are especially common in the elderly patient with advanced failure. Interesting manifestations are true vertigo, headache, and neuralgic pains about the face and in the extremities. A recent report by Zimdahl [25] mentions that potassium therapy given for a toxic arrhythmia also cleared the yellow vision which was present.

Excitability of the myocardium is increased by small doses of digitalis but is decreased by large doses, and this decrease goes hand in hand with increasing ventricular arrhythmia due to toxic doses. Toxic doses of digitalis increase the automaticity of the heart, which permits the occurrence of ectopic foci; and conduction is slowed. Thus ectopic foci tend to be isolated from one another, resulting in progressive chaos and eventual ventricular fibrillation.[26] The refractory period of the A-V node is prolonged by digitalis through its vagus effect, in small doses; this effect can be abolished by atropine. In large doses digitalis affects the node directly, and this effect is not abolished by atropine. Thus various degrees of A-V block may result from toxic amounts of the drug. It is probable that the vagal effect of digitalis is mediated by acetylcholine since this substance and digitalis share the properties of slowing conduction in the heart, and of producing intracellular loss of potassium and gain in sodium.[5] Moreover it has been shown that stimulation of the vagus releases acetylcholine within the myocardium.[27] Such a relationship may account for the slowing by digitalis of the ventricular pacemaker in complete A-V block. Atropinization might be expected to prevent this acetylcholine effect. The cardiac manifestations of digitalis toxicity result from increased irritability (or automaticity), or depressed conduction, or from combinations of these: thus almost any arrhythmia and conduction disturbance is possible. Only bundle branch block is rare as a toxic effect.

A particularly difficult situation may arise when paroxysmal atrial tachycardia at a rate slightly faster than the existing rhythm occurs; here more digitalis may lead to an increasing rate, then A-V block, with irregular ventricular rhythm, finally simulating impure flutter or rapid fibrillation. More digitalis may seem to be indicated, and may result in a fatality.[28] Bidirectional ventricular tachycardia is an uncommon though characteristic manifestation of severe toxicity. Zimdahl has discussed its treatment with potassium and gives an interesting interpretation of its mechanism.[25]

Progression of the heart failure may be the only sign of toxicity. Initial treatment is obviously to withhold digitalis, and to resume it only when the symptoms are all absent, and then in smaller doses, inasmuch as the recently poisoned heart seems to have decreased tolerance for digitalis. Serious toxic states call for prompt correction of the predisposing factors, especially electrolyte disturbances mentioned earlier. Electrocardiographic monitoring and bedside availability of supportive agents, vasopressors, vasodepressors, cutdown set, oxygen, sedation, are all necessary throughout the crisis of major digitalis toxicity. The relationship between digitalis effects and potassium changes provides the basis for the nearest approach to specific therapy for toxic states. Most if not all of the arrhythmias are apt to respond to sufficient quantities of this cation. The following recommendations are made by Lown and Levine for the use of potassium.[4] In the ambulatory patient with mild toxicity, give 5 to 7.5 grams of potassium chloride orally per day; for more severe cases give 5 grams as a stat dose, then continue it in divided doses. As prophylaxis in the use of mercurials, give 5 to 7.5 grams the day of and the day after each injection. If the patient is acidotic use the citrate or the acetate instead of the chloride. In the acutely or severely ill patient they prefer to give the potassium salt intravenously. They use a solution containing 40 mEq. in 500 cc. of 5 per cent glucose in water, given over a period of

one hour, under electrocardiographic surveillance. This is repeated once or twice, if necessary, and is followed by oral maintenance. These authors reiterate that serum levels of potassium are not necessarily low when body potassium is depleted. They caution that oral potassium is capable of producing potassium toxicity even in the absence of anuria, and they feel that congestive heart failure without digitalis toxicity is not an indication for potassium therapy. This would seem to be sound advice because it is easy to see how indiscriminate or enthusiastic attempts to titrate digitalis and potassium against each other could result in grave confusion if not disaster.

Another agent of great value in toxic states is procaine amide. It is most useful in ventricular tachycardias, and is indicated when potassium is not at hand, or if this cation has failed. It may be given orally in doses of 0.5 to 1.0 grams with additional quarter gram doses hourly for several doses, and every six hours as a maintenance. Emergency intravenous use is practical, being given as a continuous drip at the rate of 25 mg. per minute, but reducing this rate by half after 300 mg. have been given. A maximum dose of 1.0 gram in one hour is advised. Hypotension from this drug is frequent and at times alarming; therefore, the blood pressure must be watched continuously, and the drip slowed or stopped promptly as needed. A vasopressor, preferably levophed must be at hand when procaine amide is used.

In conclusion I would like to say that digitalis with its many intriguing effects, with its complexities, its dangers, but most of all its great value in prolonging useful or at least more comfortable life, continues to hold its role as the physician's most fascinating ally and his most fortunate companion.

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PREGNANCY FOLLOWING PULMONARY RESECTION *

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SHREVEPORT

Thoracic surgery in recent years has made great strides and an ever increasing number of patients who have had pulmonary and cardiac surgery are now presenting themselves for obstetrical care. The triumvirate of "blood, anesthesia and antibiotics" plus improved techniques have broadened the horizon of chest surgery. As yet the literature is rather meager in regard to the number of patients who have had pulmonary resection and subsequently delivered. In 1956, Foley, Wesp and Reichman [1] added two cases to the 62 which they were able to find in a survey of the literature. Any additional experiences in managing these patients would be of value.

MATERIAL

During the period from 1950 to 1956, we have had 9 patients who underwent pulmonary resection and subsequently delivered on 14 occasions. Undoubtedly, other patients have become pregnant and delivered in outlying districts. Confederate Memorial Medical Center is an 850 bed general hospital with an affiliated 150 bed tuberculosis unit. In northern Louisiana it serves as a primary referral center for indigent tuberculous patients who require thoracic surgery. After their convalescent period is over many of these patients are returned to their original tuberculosis hospital and follow-up in regard to obstetrical history is not readily obtainable.

The historical aspects of this subject have been amply detailed by previous workers.[2-4]

Six of our patients had a lobectomy and the other 3 had a segmental resection. In all instances the surgery was undertaken because of tubercular lesions. Because of the factors enumerated in the foregoing paragraphs our figures are weighted with patients with tuberculosis. Admittedly, other complications usually entailing thoracic surgery, e.g., lung cancer, are infrequent in females in the childbearing group.

We have not included any thoracoplasties in this study as it has been well established that pregnant patients who have undergone thoracoplasty tolerate pregnancy well.[3-5]

Pulmonary resection preceded the subsequent pregnancy by eleven to thirty-eight months and the patients ranged from 17 to 39 years of age and 7 were multiparous. Labor and delivery were uncomplicated and 14 healthy viable infants were obtained. A minimum of analgesia was used during labor and delivery was accomplished with local pudendal block or no anesthesia.

The anticipated complicating factor was dyspnea. None of our patients experienced severe dyspnea, and mild to moderate dyspnea was noted in only 3 of the 14 pregnancies.

To date we have had no cases of pulmonary resection during pregnancy which later delivered here. However, pulmonary resection has been accomplished successfully during pregnancy in a limited number of cases.[1]

DISCUSSION

We are in accord with the impressions of other workers that the pregnant patient who has undergone prior pulmonary resection tolerates pregnancy well. Patients who have undergone pneumonectomy may be more susceptible to respiratory difficulty. Dyspnea of any significance was not apparent in our 9 cases who had previous lobectomy or segmental resection. The pregnant patient who has undergone pulmonary resection compensates for moderate pulmonary insufficiency by increasing her tidal volume and is not prone to experience dyspnea.[3] In general our patients tolerated pregnancy so well and offered so few complaints that more frequent visits or special tests were not deemed necessary. One cannot deny that studies of pulmonary function prior to and

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during pregnancy would be of aid to confirm one's clinical impression.

Succinctly, Gaensler's statement that "patients with restrictive ventilatory insufficiency, who are not dyspneic at rest or during slightest exertion should tolerate pregnancy without difficulty", affords a clinical yardstick.

SUMMARY AND CONCLUSIONS

1. Nine cases of pulmonary resection with 14 subsequent pregnancies and deliveries have been presented.

2. Pregnancy was tolerated without difficulty except for mild to moderate dyspnea noted during 3 pregnancies.

3. These patients offered amazingly few complaints and no unusual precautions or special tests were deemed necessary.

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ACUTE BLOOD LOSS

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SHREVEPORT

Acute blood loss is one of the major catastrophes to which the body reacts by manifesting certain signs and symptoms which we have come to know as shock.

Before going into blood loss specifically, it is well to review the physiology and clinical picture of shock. Shock is a symptom complex which can be initiated by many causes, all of which lead to a decrease in the effective circulating blood volume. The following pathological conditions will cause shock: (1) Failure of the heart to be an efficient propelling mechanism as in heart failure or cardiac tamponade. (2) Extreme internal fluid shifts removing fluid from the intravascular space as seen in burns, crush injuries, toxins acting on the blood vessel wall, and electrolyte imbalance. (3) Hemorrhage.

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MAJOR PHYSIOLOGIC CHANGES

The following are major physiological changes, all or any of which may be present during shock:

I. Reduction of the Effective Circulating Blood Volume.

In shock from blood loss or fluid shifts, there is a decrease in the circulating blood volume. A direct relationship has been found between the reduction of blood volume and the severity of shock. Evans [4] found in using his Blue Dye Method that signs of shock usually do not appear until the blood loss is 15 per cent of the total volume and severe shock is present after reducing the volume by 38 to 40 per cent.

II. Reduction in Cardiac Output.

There has been found to be a reduction in the cardiac output in patients in a state of traumatic shock based on a failure of the venous return to the right auricle. Cardiac tamponade or myocardial contusion also may lead to a reduction in the ability of the heart to circulate blood.

III. An Alteration in Peripheral Circulation.

In the early stages of shock there has been found a definite vasoconstriction which shunts a large per cent of the blood away from the capillary beds of nonvital organs, thereby decreasing the volume of the vascular bed. This mechanism aids in maintaining a normal blood pressure.

IV. Abnormal Humoral Factors.

The studies of Zweifach, et al,[11] have brought to light this humoral concept. These investigators demonstrated vasoexcitatory material (VEM) present in the blood stream during the early reversible phases of shock and vasodepressor material (VDM) present during the irreversible stage of shock. VEM is thought to be produced by the kidney during anoxia and VDM by the liver and to a lesser

extent by the spleen and muscle under the same conditions. VEM is thought to be largely responsible for the vasoconstriction during the compensated phase of shock. During this stage, when the liver is well oxygenated, it is thought that the VDM is inactivated by the liver. As shock progresses and the liver becomes anoxic, it loses its ability to inactivate VDM and the accumulation of this substance plays a part in shock becoming irreversible.

V. Presence of Bacterial Toxins.

It has been shown that filtrates of *Clostridium welchii,* when injected intravenously, cause a shock-like picture. Some investigators have felt that the irreversibility seen in hemorrhagic shock is due to the proliferation of these or other organisms in the anoxic liver or muscle.

SYMPTOMS

The symptoms of shock are well known to all of us. In the far advanced case, one finds the patient cold, clammy, gray in color, with a rapid, thready pulse and a blood pressure that is low and sometimes not obtainable. If the blood pressure is obtainable, there is usually a low pulse pressure. In patients who are on the verge of going into shock, movement of the patient from the bed to the x-ray table or elevation of the head of the patient may cause a profound drop in blood pressure. The veins will usually be empty. It is difficult to detect early criteria of shock and great stress should be placed on the type of injury sustained. Patients with major fractures, for instance, even without external blood loss, will almost always go into shock if not treated with blood replacement. Probably the most readily available physical finding that is found to correlate most often with shock is the simple reading of the blood pressure. The first change is the decrease in the pulse pressure followed by an actual drop of the systolic pressure to figures below 100 mm. of mercury.

LABORATORY

The laboratory offers little help in the early recognition of shock. Ideally, a determination of the blood volume would be of the most value but this is not a practical test to be done on the severely injured patient as an emergency procedure except where radioactive studies are available. The red cell count and hemoglobin determination are both easily and rapidly obtained in any laboratory. However, there is some confusion in the literature as to their interpretation within the first hour after blood loss. It is the opinion of many that neither hemodilution nor hemoconcentration begins before the first one to two hours. If this be true, then these determinations done within the first hour would be of no value because, though the total blood volume is reduced, any sample taken would have a normal hemoglobin concentration and number of cells per cc. Cole and Elman [3] state in their text that in dogs hemodilution begins within the first hour. They note though that there is insufficient data to indicate the exact time of its onset in man. Despite the conflicting ideas as to the value of the early hemoglobin and red cell determination, recent experience has led me to adopt the following opinion. If these tests are within normal limits, they are of little help in determining the volume of blood lost. However, if they are definitely below normal, that is, below 10 Gms. of hemoglobin and 3.5 million red blood cells, severe blood loss is indicated and the ultimate prognosis guarded. If there is no visible blood loss, one must search for and find concealed hemorrhage.

TREATMENT

There are, of course, certain priorities in the treatment of the injured patient and these must be followed whether blood loss is present or not. Of primary importance are an open airway, and the stopping of all gross hemorrhage by either direct ligation or pressure dressings. The alleviation of pain should be accomplished by intravenous narcotics given in small doses and repeated only as necessary to avoid cumulative effects.

Many times there is considerable difficulty in accomplishing a satisfactory venous puncture on a patient in profound

shock. In these cases, one can insert a thirteen to fifteen gauge needle into the femoral vein in the inguinal region as one would in doing a femoral puncture to obtain blood. A suitable polyethelene catheter is then threaded through this needle up into the iliac veins and the needle removed. Unless one has the proper needle and the proper size polyethelene tubing always available in the emergency room, this method is not applicable and the routine cut down on the medial aspect of the ankle is probably the most satisfactory procedure for rapidly initiating intravenous therapy.

There are some advocates of intra-arterial transfusions.[10, 13] However, I believe the preponderance of experimental evidence [5, 6, 8, 12] now indicates that the rate of administration is of more importance than the route. In severe shock, blood should be given rapidly under pressure until the clinical signs improve. This can be done either by producing a positive pressure in the blood bottle or by pumping it in with a syringe and a three-way stop cock. If positive pressure is produced in the blood bottle, constant attention is required to keep air from being pumped into the patient.

Where blood loss is only moderate and the patient not in shock, glucose and saline are suitable as initial treatment while cross matching blood. When shock is more severe, some colloid solution is required for emergency treatment. It used to be that plasma was given under these conditions and it was found to be a very suitable temporary measure. However, it has three drawbacks. One is its potential for causing serum hepatitis. Secondly, its supply is limited and, last, it is expensive. In the last five to ten years, a great deal of experimental work has been done in finding and developing blood and plasma substitutes for stock piling in case of mass casualties. The two most commonly used at the present time are Dextran and Polyvinylpyrrolidone, known as PVP. Both of these substances are easily available commercially, considerably cheaper than plasma, easily sterilized and have no hepatitis potential. They are in no way to be thought of as true substitutes for blood, but only as emergency agents to be used until blood can be typed and cross matched. In this role, they are found to be extremely useful, producing a rapid and satisfactory elevation of blood pressure in the shocked patient. At the present time, both are being extensively studied for undesirable side effects. There are some reports in the literature indicating a rare bleeding tendency following usage of large amounts of Dextran. Nittis,[7] et al, reported no significant bleeding time changes when the amount was kept below 1500 cc.

Seegers, et al,[9] in an in vitro study, indicated that Dextran inhibited the formation of a prothrombin derivative. However, this was counteracted by the addition of a very small amount of thrombin which should be present in the average patient. Much more work on this aspect must be done before this is clarified. Recently, a study [1] has revealed that between 35 and 50 per cent of PVP is stored in the body for at least twenty months. It has been found in the spleen, lymph nodes, liver, bone marrow, adrenal cortex and, occasionally, in almost all organs. As yet, there has been found no definite evidence of damage from the storage of this chemical, but there was some question in one study of a slight impairment of the hepatic function. Both of these products have been used extensively and serious complications are so rare that they are considered safe for clinical use.

The rapid infusion of 500 to 1000 cc. of Dextran has, in my experience, been satisfactory to maintain all but the most profoundly shocked patients until suitably matched blood is available. However, when hemorrhage is severe, low-titer type-O, Rh negative blood may be given without cross matching, but this should be done only as a life saving procedure. Since that type of blood is seldom obtainable, blood can also be given on type, that is, take time to type the patient and, if necessary, give

his type without cross matching or on a short cross match.

The indication for vasopressor drugs in the treatment of shock is very limited. The only drug in my experience which has been effective is nor-epinephrine or Levophed, as it is commercially known. There are two indications for its use. First, it can be given to tide the patient over until adequate blood is available. Secondly, it will usually restore blood pressure to a satisfactory level when shock is so profound that the pressure will not stay up despite massive transfusions. This, unfortunately, is not always permanent. The rate of administration is always governed by the response of the blood pressure. It should not be given over long periods of time in the leg veins if other sites are available, because it may cause a slough or even loss of an extremity.

Intravenous Cortisone is another adjunct which is sometimes very useful in profound shock and should be given to all cases not responding to usual measures.

The anoxic liver has been indicted in the production of irreversible shock through the production and inability to inactivate VDM and the possible proliferation of *Clostridium welchii* within its biliary radicles. On the basis of these concepts, intravenous sodium dehydrochlolate, which has been found to increase the arterial blood flow through the liver, is of theoretical value and may be tried in severe shock. Antibiotics are also indicated.

The ideal treatment of hemorrhagic shock is, of course, adequate amounts of typed and cross matched blood. It is the only solution capable of transporting oxygen in the body and, at the same time, adding a protein rich fluid which will maintain a permanent expansion of the blood volume. The volume of blood required will vary with the type of injury and the amount of blood lost so that it is difficult to set rules for replacement. As a general rule though, correlating with Evans' findings on blood volume studies, mild shock indicates a loss of approximately 1000 cc. of blood and severe shock, a minimum loss of 2500 cc.

Massive blood replacement is not without its complications. There has been much discussion of citrate intoxication. In a recent study of patients receiving large quantities of blood, Bunker, et al,[2] concluded that the greatest danger from citrate intoxication was in the following groups of patients: (1) those with severe liver disease; (2) those with mechanical obstruction to the hepatic blood flow; (3) in infants receiving exchange transfusions; (4) in patients operated under hypothermia; and (5) those requiring rapid resuscitation with huge quantities of blood.

The action of an increased citrate blood level is to decrease the level of ionized calcium which may cause tetany and, by direct action on the heart, cause hypotension. In the above noted study, the patients with elevated Lee-White coagulation times could not be correlated with a depression of the ionized calcium. They felt that the defects in the coagulation mechanism seen in massive blood replacement were more likely due to the almost total absence of platelets and the diminished titer of prothrombin accelerator in stored blood. They concluded that intravenously administered calcium is not very satisfactory in the treatment of citrate intoxication and that when the possibility of intoxication can be anticipated, some anticoagulant other than citrate should be used.

There is no general agreement that calcium is not of value however, and, in my opinion, it should be given. Some cases have shown a remarkable response to it. The required dosage is almost impossible to determine. It lies in the range of 10 cc. of 10 per cent calcium chloride or gluconate for each 3 to 5 units of blood. It should never be added directly to the blood since it would cause clotting in the bottle.

Mismatched transfusions are probably most common in the rush of resuscitating a patient in shock. A complete discussion

of this complication will not be attempted in this paper. I would like to emphasize, however, the difficulty sometimes encountered in recognizing a transfusion reaction in the profoundly shocked patient. If any question of one arises, it is a simple matter to take a sample of blood, centrifuge it, and inspect the serum for evidence of hemolysis as indicated by a red discoloration.

As we all know, there is a direct relationship between the length of time blood has been stored and its potassium concentration. In view of this, the danger of potassium intoxication should be kept in mind. The only patients in whom this would be a factor are those with existing high potassium levels as seen in the crush syndrome and renal shutdown. In cases of this sort, only blood less than three days old should be used if possible.

Finally, overloading patients with blood with the ensuing congestive heart failure is, in some cases, a difficult complication to avoid. In massive hemorrhage with no response to blood replacement, it is difficult to know how much blood to give rapidly. When signs of heart failure appear, such as rales, pink, frothy sputum, and elevated venous pressure, one must, of course, stop transfusions and initiate the usual treatment for failure. If these symptoms appear in a patient who is still in shock, the prognosis is all but hopeless.

SUMMARY

In summary then, acute blood loss of great magnitude carries a very guarded prognosis. A rational treatment of this condition requires an understanding of the basic physiology of shock, as well as familiarity with the use of plasma, plasma substitutes, whole blood, and other drugs which may be indicated, such as Cortisone, Nor-epinephrine (Levophed), and antibiotics. We must finally know the complications arising from the use of the above agents and be prepared to treat them as they arise.

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CLINICAL USE OF THE ARTIFICIAL KIDNEY

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The artificial kidney is a standardized therapeutic procedure that has become one of the tools of modern medicine. Its use is no longer limited to research, but instead, it has benefited patients from 1½ to 80 years of age. It is a powerful tool of unquestionable value which in its present form involves only a slight risk. The actual procedure does not involve the patient's own kidney, but is instead a method of "washing" the blood and thereby removing "wastes" from the body. By many measurements, such as the removal of urea, the man-made apparatus is as efficient as the natural kidney. Clinically, the man-made apparatus is quite capable of keeping a patient without kidney function alive for considerable lengths of time. Perhaps it is not effective in completely replacing the natural kidney, but attempts at permanent replacement by kidney transplant or by plastic prosthesis appear encouraging. Certain phenomena of uremia, e.g., the anemia and the weight loss, are refractory. The length of the present use of the procedure is usually limited by technical factors. These are constantly being improved.

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All of the artificial kidney methods depend upon the same principle of physical chemistry that Abel used in 1913.[1] The wastes are removed by dialysis. This can be illustrated as follows: A membrane of cellophane has tiny, submicroscopic holes in it (Figure 1). These holes are large

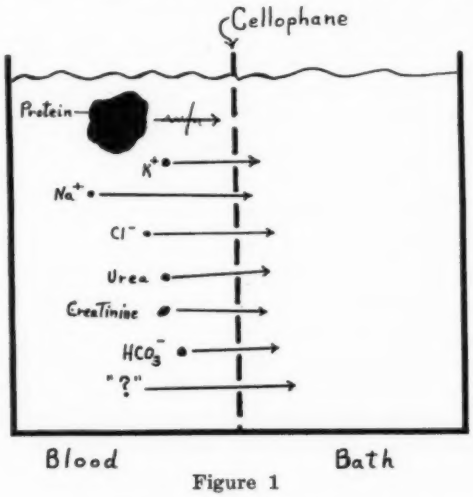

Figure 1

enough to let urea, NPN, potassium, and sodium through, but are not large enough to let proteins (albumen, globulins), or blood corpuscles pass. If the blood is on one side of the cellophane, and water is on the other side, the urea of the blood will go through the cellophane into the water. To prevent essential salts like sodium chloride from leaving the blood, a salt solution like Ringer's is used instead of water. In this way there is the same concentration of sodium on each side of the cellophane, and from the start of dialysis it enters the blood as fast as it leaves (Figure 2). Albumen, globulins, red cells, white cells, and platelets do not leave the blood, and bacteria cannot enter through the cellophane. Thus, only small molecule wastes and nonessentials leave the blood and enter the bath water. This "washes" the blood.

Cellophane sheets and cellophane tubing (common sausage casing) are used outside the body; the peritoneal membrane can be used. The bath is 100 liters of tap water with sodium chloride, sodium bi-

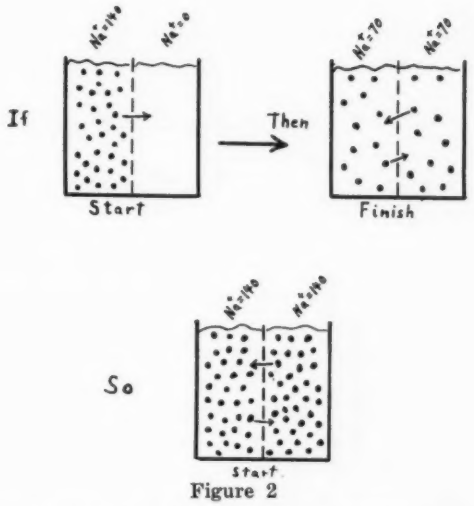

Figure 2

carbonate, carbon dioxide, calcium chloride, magnesium chloride, and glucose added. It is sterilized only when the peritoneum is used.

Of the many variations used,[2] one is probably the most valuable, and has virtually replaced the rest. This method involves the circulation of blood outside the body. Blood is continually withdrawn from an artery or vein, passed through a plastic tube, then through a cellophane tube, and to another plastic tube to conduct it back into a vein. Thus a continuous flow of blood is "washed" while in the cellophane tube. In this system the blood acts very much like water in an automobile cooling system; it carries urea and other wastes from the body to the apparatus and returns to the body to pick up more waste material. The blood flows at a rate of about a pint every two minutes. Though the body may contain only 13 pints of blood, 180 pints flow through the apparatus in the usual six hour period, or, all of the patient's blood goes through the apparatus an average of about 15 times. The blood does not clot because of the heparin added.

Of the other methods used, peritoneal lavage, or dialysis across the peritoneal membrane,[3] is probably the most effective. Twenty liters of sterile Ringer's solution is passed through the abdominal cavity daily. The procedure is carried on day

and night, perhaps for days. Besides the hazard of infection, it takes days to do what the above procedure will do in hours. It is no longer more effective than the cellophane method in removing edema, and is certainly less desirable.

Intestinal lavage is effective in removing potassium. It fails to help the patient in renal failure to any great extent, and usually results in giving the patient large quantities of water, which is undesirable. This same removal of potassium can be had by simple gastrointestinal suction, or by other means.

The present apparatus is simple,[4] compact, and stored sterile, ready to use. It can be moved and requires minimal upkeep. It has all of the advantages of the earlier Kolff rotating drum apparatus, and by design has eliminated most of the technical hazards, as follows. Because of the pressure relationships, a leak in the cellophane would not allow entry of unsterile bath water into the blood as in previous equipment. Because of the pumping arrangement, the circuit can be made from vein to vein. This eliminates the necessity of an arterial cutdown, and, more important, the risk of removal of arterial blood from a seriously ill patient. This taking of even a small part of the critically low output of a failing heart has been fatal in many instances in the past. It is now possible to remove large quantities of water (edema) from the body by high pressure ultrafiltration, thus matching the previously held advantage of peritoneal lavage.

PRESENT CLINICAL USES

The procedure of the artificial kidney has proven itself in acute renal failure ("lower nephron nephrosis"), drug poisoning, some situations in chronic kidney failure, and as a stepping stone for further procedures, such as the transplanting of the human kidney. It may prove to be of value in shock and in acute glomerulonephritis.

ACUTE RENAL FAILURE ("LOWER NEPHRON NEPHROSIS")

The treatment of acute renal failure remains the principal use of the artificial kidney. This includes the kidney shutdown that may follow:

1. Shock from bleeding or from any other cause
2. A transfusion reaction
3. A crush injury without hypotension
4. Surgery without shock
5. Heavy metal poisoning, e.g., mercury or bismuth
6. Carbon tetrachloride poisoning, in association with liver damage (and thereby little rise in BUN)
7. Hemolysis of an illness, or of the infusion of distilled water (e.g. during a transurethral prostatectomy)
8. Postpartum (including perhaps the syndrome of renal cortical necrosis as a variant)

All of these causes provoke a similar kidney damage and clinical picture.[5] They differ in the severity of the kidney damage and in the nature of the provoking illness. Almost all of this group of patients will show signs of return of their own kidney function within three weeks, should they survive that long. The mildest will only fail for a few days. Everyone can recall a memorable case that survived twenty days of oliguria, but these few cases are distinctly the exception. The vast majority have either started passing urine or have died by the tenth day. About 50 per cent of the cases do each. An infection or the presence of damaged tissue greatly hastens the decay of the patient and may bring about full blown "uremia" in three to four days. These burdens should be vigorously treated by antibiotics and debridement. Conversely, the presence of kidney failure renders the patient incapable of resisting an infection and unable to heal his wounds.

All patients with acute renal failure should be treated by the conservative regime.[6] This consists of three essentials: (1) controlled restriction of water intake, (2) a high calorie, no protein intake, and (3) measures to control serum potassium. To this one may add a fourth, the maintenance of a fairly normal serum sodium.

Water is restricted to 500 cc. plus a replacement of loss by suction and the urine volume when significant. Dehydration is to be avoided; it mimics the syndrome of uremia. Gastrointestinal suction will remove significant quantities of water and potassium, and thus allow the giving of extra glucose in water intravenously.

A high calorie intake, or really a 1000 calorie intake, is designed to delay tissue breakdown, and thus inhibit the progress of uremia. Patients with acute renal failure will lose weight in spite of 2000 calories a day as glucose. It is the feeling of most observers that 100 grams of glucose a day gives about as much benefit as 400 grams. No good studies are available on this point. Butter by mouth is limited by vomiting, and those who laud its use exclude any patient who vomits. Its absorption in patients not so ill is questionable. Intravenous 10 to 50 per cent cottonseed oil emulsion can be used. About 500 cc. of 20 per cent glucose per day is the usual.

Potassium restriction should be as complete as possible unless the patient clearly shows that a high serum potassium will not be a problem. This includes the use of sodium penicillin instead of potassium when high doses are wanted.* Two million units of K^+ penicillin contain about 3 milliequivalents of potassium. About half of the patients in acute renal failure have a significant rise in serum potassium, but only a few of these manifest potassium intoxication.[7] Most deaths under good conservative management will be without potassium intoxication. The electrocardiographic changes are well known; they progress from an elevation of the T waves (with symmetry of the upswing and downswing) to prolongation of the PR and QRS intervals, then a voltage decrease, and then standstill. The rise in serum potassium can be aborted by the use of resins (e.g. SKF #648) either orally or as enemas.[8] Gastrointestinal suction impedes it; intravenous glucose and insulin temporarily lower it; digitalis, sodium, and calcium pharmacologically antagonize it. Calcium is very predictable, but also limited. An intravenous calcium gluconate drip is a dependable way to gain time in serious potassium intoxication, in order to do something more lasting.

The serum sodium may be low as a result of the dilution by intravenous glucose in water (containing levophed or such) given during the initial shock that caused the renal failure or immediately postoperative. The author believes that the serum sodium should be maintained near normal for three reasons. An occasional hyponatremic patient in acute renal failure will get enough return of renal function with hypertonic sodium by vein to make the difference. Azotemia of the hyponatremic syndrome can be mistaken for acute renal failure. The rise of potassium is more serious if the sodium is low.

It is when the conservative regime alone fails that the artificial kidney finds its place in about half of the cases. When the decision is difficult, it is far wiser to use the artificial kidney than to wait, as it is difficult to predict exodus in this disease. The serum potassium and the electrocardiogram should be carefully followed to predict exodus from hyperkalemia, but this is not the common way of death; and after one run on the artificial kidney, it is rare. Congestive heart failure is common; it is aggravated by any excess of water given. In the cases during World War II, it is described as the commonest cause of death and occurred on about the seventh to eighth day.[9] This has since been explained as a result of the excessive amounts of water given in those days. Perhaps this is not the sole cause of congestive heart failure; it is often noted to come on overnight and progress to severe pulmonary edema very quickly, in spite of the fact that no water had been given in twenty-four hours! One will find aminophyllin and parenteral digitalis somewhat effective, but a phlebotomy

* The sodium salt should also be used in other forms of renal failure, chronic or so called "prerenal azotemia", when high doses are called for. It is available from Eli Lilly, Indianapolis.

of 300 to 800 cc. more so. After rescuing the patient from this hazard, he is frequently in dire straits within twenty-four hours from the rest of the picture of uremia. The advent of congestive heart failure, then, is an evidence of impending death. The author has found that the quality of the mitral first sound at the apex is a good index of the patient's status. As the patient declines, it loses its crispness and becomes muffled as it does in rheumatic or diphtheritic myocarditis. Most often the patient will expire suddenly, in the middle of a sentence. He will have been jittery and restless, with a short interest span for two or three days. For two or three nights he will not have slept, except for catnaps with the light on. In the few patients the author has had occasion to observe terminally, the blood pressure rapidly falls in the conscious patient to unobtainable levels, and then the patient suddenly drops off. The pupils may dilate while he speaks. It is the picture of a rapid central shock as in a massive coronary, a large pulmonary embolus, or cardiac arrest. The electrocardiogram in those instances recorded at the time, shows a relatively normal pattern to continue after clinical death (loss of consciousness, pulse, respiration, and blood pressure), thus virtually ruling out cardiac arrest. Post mortem examination fails to show the embolus in the lung. Perhaps this is severe "forward heart failure," a day or two after "congestive heart failure". If the patient is very ill with uremia, the taking of arterial blood, i.e. even a small part of the heart's output, will precipitate the same irreversible shock. Dialysis, vein to vein, has been lifesaving. A successful run on the artificial kidney will strikingly restore cardiac function.

Unless there is some associated heart disease, the mitral first sound at the apex will sharpen to normal within about an hour on the artificial kidney, and a gallop will often disappear in that time. The general appearance of the patient will usually show a striking change. He will appear less ill; he will become more attentive to his surroundings and maintain a normal interest span. Vomiting quickly subsides, then nausea; it is not unusual for an appetite to appear after four to five hours of effective blood flows. By auscultation, intestinal peristalsis, which had been virtually absent for two to three days may appear and become normal. He then sleeps well; frequently he will have a normal bowel movement the next day. Essentially, after the deterioration of seven days of severe oliguria, the patient has become clinically and severely uremic. The artificial kidney is used for six to eight hours, and the patient is clinically improved to about where he was on the second day. He then is allowed to repeat his decline under observation and conservative therapy, and the artificial kidney is again used. This cycle, barring mishaps, is repeated on and on until his own kidneys start to function. Most patients with the "lower nephron nephrosis", if kept alive this way for three weeks, will have a return of their own kidneys. In those clinical situations in which no return has occurred in three weeks, the disease is probably something else. During this three weeks an infection may subside, and the patient may decline less rapidly. Should an infection get out of hand, the benefit of the artificial kidney may be spent within a single day.

Dialysis is no longer necessary when the patient's own kidneys take over. This too is difficult to judge. It is not unusual to see a patient clinically deteriorate while putting out 2 liters of "urine" a day. Urine concentration is not a valid gauge; it will remain low for three or more weeks after the diuresis starts. Should it take five days for the patient to start to "open up" (i.e. pass 500 cc. or more urine), then he will start to "break even" a day or so later. If he "opens up" slower, the delay is longer. If it takes twenty days to cross the 500 cc. mark, then it will be three to four more days before he stops deteriorating. Death during these days is not unusual. Lastly, a peculiar situa-

tion occurs. It is distressing and should give a clue to the mechanisms of the disease. Occasionally, a patient will start diuresing late, excrete 500 cc. on the twentieth day, 2000 on the twenty-third day, and 3000 cc. of "urine" on the twenty-fourth day. On this day he will have a return of some appetite, will look better to the nurses, and will volunteer that he feels much better. His NPN, serum potassium, and such will be considerably lowered by his diuresis. Then he suddenly drops dead. In the author's experience, two subtle, ominous signs were still present. The patient was still jittery; his interest span was short; he was restless, and did not sleep the previous night. His mitral first sound had remained muffled. One more run on the artificial kidney would, in all probability, have been the difference.

Statistics of survival of patients who require the artificial kidney are not valid. They depend primarily upon the illness which caused the renal failure, the concurrent illness, and the selection of cases to run.

The following cases will serve to illustrate the use of the artificial kidney in "lower nephron nephrosis". The first case in Louisiana, in 1954, is a simple example (Figure 3).*

The patient, a 34 year old white female, in previous good health entered a local hospital in shock associated with bleeding of an abortion. In the emergency she was given several liters of intravenous glucose in water, a pint of mismatched blood, and a D and C was done. The next day she was noted to be severely oliguric. During the next thirteen days she was treated conservatively. On the fourth day she was given hypertonic salt, raising her serum sodium, and there was an associated slight rise in urine output. Her weight remained at 144 pounds, although she started to have edema. Serum potassium did not rise above 5.5 meq/li. at any time; BUN and creatinine rose steadily. She became progressively ill, began vomiting on the sixth day, had petechiae on the twelfth day, and became dyspneic on the

* The author is indebted to Dr. Adolph Jacobs, Chief of the Independent Ob-Gyn. Service at Charity Hospital, for the presentation of this case.

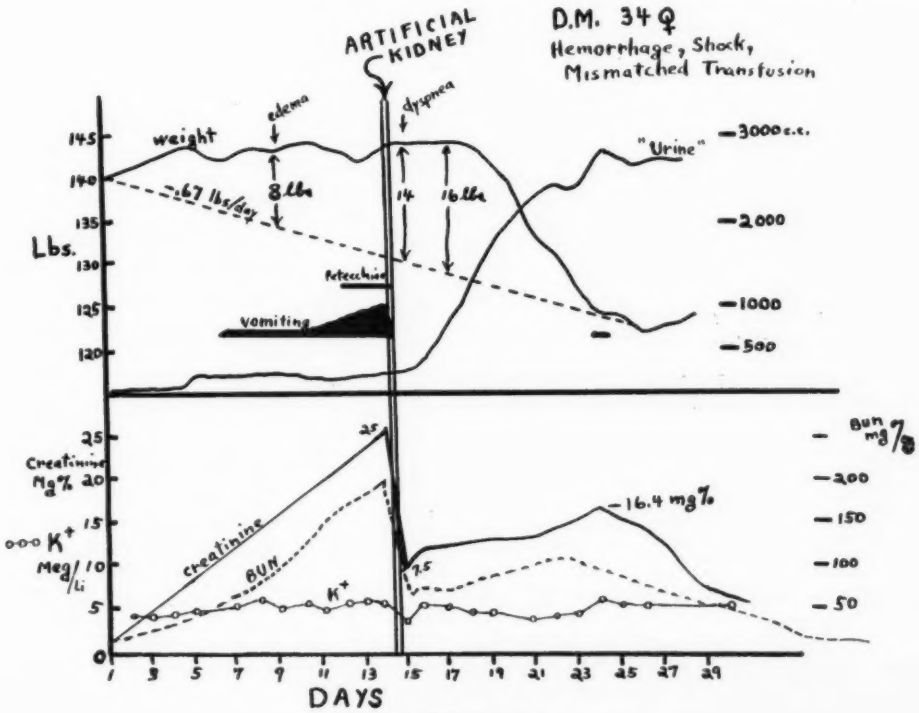

Figure 3

thirteenth day. At that time she was still putting out 150 cc/day of "urine". The artificial kidney was used for eight hours on the fourteenth day. She appeared strikingly better; nausea and vomiting disappeared; she regained her appetite. Her heart sounds improved to normal, but she still had some evidence of congestive failure. Conservative therapy was resumed. She could eat again; no more petechiae were noted. Packed red blood cells were given for her anemia. A few days after the dialysis she started to diurese. The rise in urine output was less rapid than one notes in cases that diurese at an earlier date.

During dialysis her serum creatinine fell from 25 to 7.5, but in spite of putting out 500 cc. of "urine" on her seventeenth day, it continued to rise to a peak of 16.5 mg% on the twenty-fifth day, before it fell from her own kidney function. This demonstrated the persistence of frank kidney failure in spite of the excretion of 2000 cc. of "urine" daily. She did not become clinically ill after dialysis except for some vomiting on the twenty-fourth day. This is probably due to the fact that she had little necrotic tissue, and it took thirteen days of renal failure to reach extremis the first time. Her weight dropped dramatically during the diuresis as she lost her edema. The loss of weight was probably a steady .67 pounds a day as shown by the broken line in the graph; the difference between this broken line and her actual weight is probably water retained. At 8 pounds she manifested edema and at 14 pounds was in clinical heart failure.

This patient has gone on to uneventful clinical recovery. She rapidly regained her weight. One year later she was clinically well and had no symptoms referable to the kidney. Her creatinine clearance was 60 per cent of normal.

This case is an example of acute renal failure without tissue necrosis, who deteriorated slowly. One run on the artificial kidney on the fourteenth day was sufficient to tide her over three weeks of kidney failure. Others are not so simple.

For example, a 17 year old boy * was shot through the right thigh while playing with a new shotgun. He bled profusely, and was rushed to the nearest hospital. The bullet avulsed about 6 inches of the femoral artery and destroyed the profunda branch. It created a large ulcer on the medial aspect of the right thigh, with an exposed fracture of the femur. Though the sciatic nerve was anatomically intact, it was not functioning. Thirty pints of blood were given; an excellent emergency nylon arterial graft was sewn in to bridge the gap in the femoral artery. This restored the pulses to a bloodless right leg. The leg was placed in balanced traction; the wound was debrided and dressed.

On the second day he was transferred to the Touro Infirmary for further care. The wound was further debrided, and the position of the graft was altered. He was noted to be severely oliguric. Conservative therapy of acute renal failure was started. Vomiting was present from the start. On the fifth day he appeared quite ill. The mitral first sound had become progressively less crisp, and on the sixth day it was readily confused with the louder 2nd sound at the apex. He received only 200 cc. of fluids intravenously during the sixth night and lost the same amount of fluid in gastrointestinal suction that same night. In spite of no gain in water, he was noted to be slightly dyspneic at 7 a.m. of the seventh day. By 9 a.m. he was in frank pulmonary edema, with severe cyanosis, loss of consciousness, and a pulse rate of 150 per minute. An EKG taken at about 8 a.m. showed sinus tachycardia and slight peaking of the T waves in the precordial leads. He responded dramatically to a 500 cc. phlebotomy, and was digitalized. The intravenous was stopped, and gastrointestinal suction was continued. During the day he was awake and alert; he was not bothered by congestive heart failure. At about 7 p.m. he was noted to have an irregularity of his pulse, and he rapidly became stuporous. His blood pressure fell to shock levels, and his pulse fell to about 50 per minute. He was cyanotic and lost consciousness. An EKG showed severe hyperkalemic effects: rate 40 per minute, QRS widened to .28 per second, and multiple ventricular premature beats. (His serum potassium was 8.1 meq/li. that morning and 8.0 that evening at 7 p.m.) An intravenous infusion of calcium gluconate was immediately started with restoration of his blood pressure and EKG almost to normal. He returned from coma to stuporous state.

He was put on the artificial kidney and diayized for six hours. Within the first fifteen minutes the heart sounds had improved remarkably, and after thirty minutes, he was weaned off the calcium infusion. He became alert and rational. By the end of the procedure, his appetite had returned for the first time since he was shot. His NPN fell from 212 to 131. For the next few days it was possible to feed him by mouth, and a conservative regime was resumed. He continued to excrete 40 cc. of muddy "urine" a day. Five days after the first dialysis he was again dialyzed because of a recurrence of vomiting and poor heart sounds. He had the same clinical recovery; conservative therapy was resumed. Three days later, the fifteenth day, his "urine" output rose to 150 cc. per day. On the eighteenth day,

* The author is indebted to Drs. Robert Schramel and Edward Haslam of the Tulane Surgery Department for the presentation of this case.

although he had passed 450 cc. of "urine" in twenty-four hours, he was dialyzed a third time for the same findings. For a third time his appetite returned, and conservative therapy was resumed. Fresh petechiae were noted on the twentieth and twenty-first days. On the twenty-second day vomiting recurred. A friction rub was heard from the eighteenth through the twenty-sixth day. On about the twenty-fourth day (the sixth of his diuresis) he no longer went downhill, but slowly showed clinical improvement. On the twenty-fifth day intravenous potassium chloride was necessary for hypokalemia.

Massive doses of antibiotics, including 20,000,000 units of sodium penicillin by vein per day, were given. Wound healing was delayed. About one month after the injury, healthy granulation tissue started to grow, and bone callus was noted in x-ray for the first time. He had 2 massive hemorrhages from the wound since diuresis. This required anesthesia and surgical intervention, but he withstood the procedures well. Recovery is slow.

This is an example of severe acute renal failure, complicated by a massive wound. Each harmed the other. Uremia progressed rapidly to virtual exodus in seven days. Three runs on the artificial kidney were necessary to keep him alive for three weeks until his renal function returned. The recurrence of severe symptoms, such as petechiae, a friction rub, and vomiting, along with the neurological and cardiac findings of uremia several days after the third dialysis, proved the necessity of the third dialysis, in spite of the output of a fair amount of "urine", or apparent return of renal function. Wound healing was considerably delayed; the infected wound did poorly, but did not break down. The nylon artery graft remained intact and subsequent plastic surgery was necessary. Hyperkalemia did not threaten after the seventh day. Even when his EKG showed terminal changes of hyperkalemia on the seventh night, his serum potassium was actually the same or even lower than it had been that morning. It is evident that the electrocardiogram depends on other factors in addition to the serum potassium.

DRUG POISONING

The artificial kidney is very effective in removing most drugs from the body. Any drug of low molecular weight will diffuse through the cellophane, even if it is largely bound to proteins of the blood. To date, the method has been used clinically to remove several drugs in situations where it was desirable to remove them.

Barbiturate intoxication, when severe and out of reach of conventional therapy, can be treated this way.[10] In those cases of overdose in which the epinephrin-like drugs (ephedrin, neosynephrin, levophed, etc.) are given in doses large enough to cause side effects, such as cardiac arrythmias; the metrazol, picrotoxin, or the like are given to the extent of focal convulsions; though respirations can be supported by a respirator or electrical stimulation, the blood pressure cannot, and the urine output has fallen, the artificial kidney is still quite effective in removing the causative drug. Six or eight hours on the artificial kidney will allow removal of sufficient barbiturate to bring the patient from coma to a groggy awake state. Since it will eliminate three to four days of critical coma, and the risk of pneumonia, it should be considered in the less severe poisonings.

Bromides[11] are very rapidly removed by the artificial kidney. The clinical illness of bromide intoxication can be shortened from several weeks to a day or two by this method.

Doriden poisoning has also been quite successfully treated this way.

Salicylate[12] poisoning produces the therapeutic dilemma of metabolic acidosis and respiratory alkalosis. Should the intoxication be of any seriousness, the simple solution is to remove the salicylates via the artificial kidney.

Thiocynates, rarely used today, can cause a peculiar clinical picture, which has been very effectively treated by dialysis.

As the occasions present, many other drug intoxications will be treated by this new method.

CHRONIC RENAL FAILURE

Since the evolution of chronic renal failure is slower than the acute renal failure, it will be some time before very much is

known about the use of the artificial kidney in this disease. To date, it seems that a person who gradually has sunk into the syndrome of uremia from chronic pyelonephritis, polycystic kidneys, and perhaps chronic glomerulonephritis will get between three weeks' and six months' relief from his symptoms by a run on the artificial kidney.[13] Repeated dialyses are less effective. The result seems to be not too predictable, and it has been found that those with malignant hypertension do poorly. It is interesting that the patient may not improve for forty-eight hours after dialysis.

Should a person who is moderately uremic, but compensated, become acutely ill with an infection or as a result of necessary surgery, he may be benefited or returned to his previous state by the artificial kidney. A run on the artificial kidney will reduce the risk of surgery for bilateral staghorn calculi in the already uremic patient.

DOUBTFUL INDICATIONS FOR THE USE OF THE ARTIFICIAL KIDNEY

There is a bit of evidence that dialysis may be useful in the treatment of intractable shock. Here it would be of great advantage to have a blood circuit from vein to vein instead of artery to vein.

Peritonitis per se is not treatable by the artificial kidney. Some doubt may be raised by a recent experience.

A 42 year old woman was found to have a ruptured appendix and peritonitis when explored for an acute abdomen. Five grams of sulfonilamide was put into the peritoneal cavity at surgery. Postoperatively she was oliguric for almost two weeks. She had fever and a silent, tender abdomen. She was dialyzed on the fifth and ninth days. Though the fever persisted, she was clinically much improved and had a return of peristalsis following each dialysis. By the end of the second week she had a return of urine output and went on to full clinical recovery.

It is difficult to tell where one disease ends and another begins. It is well known that severe infections are associated with azotemia and some oliguria, not so prolonged as in this case of acute renal failure. It is interesting that dialysis resulted in the return of peristalsis in spite of peritonitis in the case mentioned. The question may be raised as to whether the infection itself could have been helped by dialysis in the absence of acute renal failure.

DANGERS OR CONTRAINDICATIONS

Bleeding is the major danger or contraindication to the use of the artificial kidney. The oozing and petechiae of uremia cease with dialysis, but the person with a peptic ulcer is prone to bleed when given heparin. Indeed, a person who spontaneously bleeds from the GI tract when heparinized probably has an ulcer. A wound over an hour old seldom bleeds.

A fresh myocardial infarction is often stated as a contraindication to dialysis. The author has never seen a myocardial infarction produce severe enough acute renal failure to necessitate dialysis. However, a myocardial infarction may occur in association with other illnesses, e.g., bowel infarction with necessary surgery, which may result in a severe renal failure. The author has successfully dialyzed such a patient using a circuit from artery to vein. Today it would be safer to use a circuit from vein to vein. Although a fresh myocardial infarction would increase the risk of dialysis, it should be done when indicated. Perhaps in the future a precedent will be set to dialyze these patients with a circuit from vein to artery. This would be the circuit of the artificial heart, since the "kidney" also aerates the blood. Thus the risk would be even less.

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THE SYSTEMIC USE OF ACTH AND SYNTHETIC ADRENAL GLUCOCORTICOIDS AND MINERALOCORTICOIDS

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HISTORICAL NOTE

The preparation of adrenal cortical biological extract by Swingle and Pfiffner,[1] in 1930, lit the dawn for physiological treatment of altered function of the adrenal cortex and ultimately led to ascendency of steroids in the management of mesenchymal disease. Highlights of the brilliance that followed are listed below.

1934: Isolation of cortical hormones.[2]
1937: Identification of desoxycorticosterone.[3]
1943: Purification of ACTH.[4-5]
1946: Synthesis of Compound E.[6]
1949: Treatment of arthritis.[7]
1953: Identification of aldosterone.[8]
1954: Preparation of halogenated steroids.[9]
Development of delta compounds.[10]

ANTERIOR PITUITARY-ADRENAL CORTICAL PHYSIOLOGY †

When ACTH is injected repetitively into humans with responsive adrenal cortices, or when high levels of synthetic 11, 17-oxysteroids are administered, profound metabolic events occur. These changes, beneficial and undesirable, are proportional to dosage and duration and mediated by tissue consequences of glucocorticoids, androgens and mineralocorticoids. Following ACTH stimulation of the cortex, all of these hormones, except aldosterone, in increased amounts are endogenously produced, but after peroral or parenteral glucocorticoids, intrinsic yield ceases or is diminished markedly.

Glucocorticoids naturally proliferated in the adrenal cortex are chiefly hydrocortisone, with small amounts of cortisone and corticosterone. They are estimable in urine or plasma and designated 17-hydroxycorticoids (17-OHC). Normal adult values for 17-OHC are: males 6-14 mg./24 hours and females 4-10 mg./24 hours when measured as Porter-Silber chromagens. Normal adult values for plasma 17-OHC by modification of the method of Nelson and Samuels are 7-18 micrograms per cent.

Mineralocorticoids naturally occurring in the adrenal cortex are desoxycorticosterone and aldosterone. The latter singularly is not regulated by ACTH. Clinically useful methods for assay of these substances have not been perfected. Their influence is primarily on electrolytes.

Androgens also are produced naturally by the adrenal cortex and measurable in urine as 17-ketosteroids (17-KS). They are metabolically weak, consisting chiefly of dehydroisoandrosterone, and approximately 1-2 mg. of that excreted in female urine come from the ovaries, while in males, about 5 mg. originate from the testes. Normal adult values for urinary 17-KS per 24 hours are: females 5-15 mg. and for males 10-20 mg. Their chief properties promote virilism and protein anabolism. Further consideration will not be given here.

Glucocorticoid Effect: Release of ACTH by the anterior pituitary is inhibited, and the adrenal cortex assumes a quiescent state, with little or no production of hormones.

Gluconeogenesis and liver glycogenesis rates are elevated, leaving a wake of stri-

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† See references 11-30 for detail concerning physiology, indications and rationale of therapy.

ae, hyperbruisability, osteoporosis, pathological fracture, metastatic calcification, and poor healing. Carbohydrate tolerance decreases and, if severe, diabetes mellitus may supervene.

Fat production, mobilization and redistribution rise; the physiognomy reveals moonface, centripetal obesity and thin limbs.

In connective tissue disease, antiphlogistic dominance halts dissolution of structural mucopolysaccharide substrates of ground substance and collagen, with resultant decreased mobility of plasma and blood cells into tissue. This leads to decreased rubor and dolor and to increased vulnerability to microorganisms.

Mineralocorticoid Effect: Hydrochloric acid production in the stomach mounts in 50 per cent of patients and is manifested by dyspepsia and occasionally by ulcer. Electrolyte shifts move potassium from cells and increase intracellular sodium. Renal excretion of sodium slows as kaluresis accelerates. The net result is hypernatremia, hypertension, edema and hypopotassemic weakness.

Central Effect: Symptoms ranging from euphoria to psychosis accompany hypercortical states.

SYSTEMICALLY USEFUL MODALITIES

A. ACTH Gel.
B. Synthetic Adrenal Cortical Steroids.‡
   1. *Oral*:
      a. Cortisone acetate (Compound E).
      b. Hydrocortisone (Compound F).
      c. Prednisone (delta ^{1} E). Former generic name: *metacortandracin.*
      d. Prednisolone (delta ^{1} F). Former generic name *metacortandralone.*
      e. Fluorohydrocortisone (FF).
   2. *Sublingual*: Desoxycorticosterone acetate linguets.
   3. *Intramuscular*:
      a. Hydrocortisone sodium hemisuccinate (F-HS).
      b. Desoxycorticosterone acetate (DC-A).
      c. Desoxycorticosterone trimethyl acetate (DC-TMA).
   4. *Intravenous*: Hydrocortisone sodium hemisuccinate.

‡ The following are investigative and not therapeutically significant at present: fluoroprednisolone, aldosterone, 2-methyl-hydrocortisone, 2-methyl-fluorohydrocortisone, and 14-hydroxyhydrocortisone.

RATIONALE OF THERAPY

ACTH: The usefulness of ACTH demands sound adrenals, for if the target organ is enfeebled or destroyed by local disease, trophic hormone is dissipated. Adrenals can be stimulated by prolonged intravenous administration of lyophylized ACTH, or by daily intramuscular injections of repository ACTH. At basal conditions the adrenals elaborate into the bloodstream an effluent of hormones (17-OHC) equivalent to 30-40 mg. of hydrocortisone daily. When stimulated maximally, production rises to 240 mg. per day.[31] If a disease requires more than this amount of Compound F for remission, it cannot be produced endogenously, and ACTH will not control effectively.

ACTH is a polypeptide, and the risk of antigen-antibody reaction is ubiquitous but small. Other frailties are: (1) it must be given parenterally, and (2) the limitation of response by the adrenal when supreme cortical effect is desired.

Synthetic Adrenal Cortical Hormones: These compounds, with the exception of desoxycorticosterone, rapidly and almost completely are absorbed from the gut. Dosage is easily calibrated. When quantities under 50 mg. daily of cortisone or hydrocortisone are employed, fluid retention is no problem, and these less expensive drugs are choice. Above that level undesirable inorganic sequelae are usually present, and the analogues prednisone and prednisolone should be used, for therapeutic effectiveness is attained at lower dosage (⅛ or ¼), although milligram for milligram they promote fluid retention in equal amounts as do the older steroids. Cardiorenal disease complications specifically demand delta compounds, and patients are especially thankful for salt liberalization, which can be permitted oftener with the unsaturated drugs. Unfortunately

TABLE 1
SCHEME OF THERAPY

Adrenal State	Example	Desired Adrenal State	Hormones of Choice	Dose (Mg./Day)	Adjunct
Hypofunction	Panhypopituitarism	Basal	E or F or ACTH*	30.0	Thyroid Estrogen (♀) Testosterone (♂)
	Addison's Disease & Post-Adrenalectomy Syndrome	Basal	E or F + FF or DC-TMA**	30.0 0.5 2.0	NaCl
	Acute Adrenal Cortical Insufficiency	Mod. to Severe Hypercorticism	F-HS + DC-TMA**	300.0 2.0	NaCl
Androgenic Hyperfunction (Elevated 17-KS)	Adrenogenital Syndrome	Basal (Suppression 17-KS)	E or F	30.0	—
Normal	Rheumatoid Arthritis	Mild Hypercorticism	Δ^1E or Δ^1F or ACTH*	20-30.0	KCl
	Lymphocytic Leukemia	Moderate Hypercorticism	Δ^1E or Δ^1F or ACTH*	30-40.0	H. Prot. Diet KCl Testosterone***
	Nephrotic Syndrome	Severe Hypercorticism	Δ^1E or Δ^1F	80-120.0	Same
	Pemphigus Foliaceus	Super-hypercorticism	Δ^1E or Δ^1F	120-250.0	Same

* Daily injections of gel with clinical response as guide to dosage.
** Given as 50 mg. I.M. every 2-4 weeks.
*** With delta compounds, but not with ACTH.

they are reported to cause a higher incidence of vasomotor and peptic symptoms and purpura.[32]

Fluorohydrocortisone acetate, because of intense sodium retention, provides adequate inorganic and vasopressor need when given in daily oral doses of 0.5 mg. in lieu of monthly, intramuscular injections of desoxycorticosterone trimethyl acetate for Addison's disease and post-adrenalectomy syndrome.

Hydrocortisone sodium hemisuccinate is assimilated so rapidly into tissue humor after intravenous or intramuscular administration that its use for perilous adrenal cortical insufficiency crises is astonishingly gratifying.

Estimation of Dosage: From above data, it may be assumed that basal requirement of cortisone or hydrocortisone is about 30 mg. daily and prednisone or prednisolone 7.5-10 mg. daily. Stressful events and disease commonly double and triple this demand. Less often four to ten, and rarely, even thirty-fold amounts are required. Basal dosage is indicated primarily for hormonal replacement, regardless of the cause.

Increments of ACTH to evoke the desired cortical synthesis of steroids is difficult to judge without measurement of urinary or plasma 17-hydroxycortoids. Therefore, unitage and injection interval must be computed from clinical parameters of hormonal replacement response or inflammatory composure.

The induction of adrenal hypercorticism is necessary to combat the ravages of most mesenchymal diseases. It is convenient to categorize the desired adrenal state as folows for purpose of adjusting dosage to equilibrium with the degree of disease:

1. Basal
2. Mild hypercorticism
3. Moderate hypercorticism
4. Severe hypercorticism

5. Superhypercorticism

All dosages if prolonged cause inactivity of the adrenals, which require a few days to reactivate after discontinuance. Levels above basal, if given for months or years, may cause severe Cushing's syndrome medicamentosa, with devastating morbidity.

CLINICAL ENTITIES RESPONSIVE TO ACTH AND/OR ADRENAL STEROIDS

(Responsiveness herein does not in every case mean preference).

I. *Hormonal malfunction*:
- Acute adrenal cortical insufficiency (Waterhouse-Friderichsen's syndrome, traumatic and surgical shock, and relative cortical insufficiency after prolonged suppression of adrenal reserve with corticoid therapy).
- Addison's disease
- Adenoma, pancreatic islet cell
- Adrenogenital syndrome
- Panhypopituitarism
- Post-adrenalectomy syndrome
- Thyroid storm

II. *Mesenchymal disease*:

A. Hematological disease:
- Anemia, aplastic
- Anemia, hemolytic
- Leukemia (acute, lymphocytic, granulocytic, and monocytic).
- Pseudohemophilic thrombasthenia
- Reticuloendotheliosis
- Thrombocytopenia
- Transfusion reactions

B. Diffuse collagen disease:
- Arthritis, psoriatic
- Arthritis, rheumatoid
- Arthritis, degenerative
- Asthma, (seasonal, perennial, bronchial)
- Bursitis
- Edema, angioneurotic
- Emphysema, pulmonary
- Erythema multiforme
- Fibrosis, pulmonary (Hamman-Rich syndrome)
- Fibrositis
- Myocarditis, allergic
- Osteitis, pubis
- Pemphigus foliaceus
- Polyarteritis nodosa
- Regional ileitis
- Rheumatic carditis, acute
- Rheumatic fever, acute
- Sarcoidosis
- Scleredema
- Scleroderma (dermatomyositis)
- Serum sickness
- Systemic lupus erythematosus
- Spondylitis, rheumatoid
- Torticollis, chronic
- Ulcerative colitis
- Whipple's disease

C. Dermatologic disease:
- Dermatitis, atopic
- Dermatitis, contact
- Dermatitis, exfoliative
- Dermatitis, herpetiformis
- Dermatitis, medicamentosa
- Dermatitis, venenata
- Eczema, atopic
- Pemphigus, vulgaris
- Psoriasis

III. *Miscellaneous*
- Carcinoma, prostatic
- Gout
- Glycogenosis (von Gierke's disease)
- Infections, overwhelming
- Lymphosarcoma
- Nephrotic syndrome
- Peyronie's disease
- Snake venom poisoning
- Sprue
- Weber-Christian disease

STEROID WITHDRAWAL SYNDROME

When patients have been treated with adrenal glucocorticoids equivalent to or more than 60 mg. hydrocortisone daily for prolonged periods, usually two months or more, and withdrawal is abrupt, an alarming syndrome may develop within twenty-four to forty-eight hours. It is characterized by weakness, nausea, vomiting, abdominal pain and generalized muscular cramps. The mechanism is due to pituitary suppression of endogenous ACTH, and although ominously masquerading as acute adrenal cortical insufficiency, the syndrome is nonfatal, because the adrenals, if present, continue to produce the powerful sodium retainer, aldosterone.

Symptoms usually subside in two to five days. This syndrome can be prevented or minimized by gradual discontinuance of steroid therapy.

Equally as important, a recrudescence of disease may, and usually does, occur, sometimes to fulminating degree. This is highly influenced by the general condition of the patient.

In order to decrease this unpleasantness, all patients on prolonged use of steroids should carry purse cards indicating diagnosis and treatment so that those who ministrate to them following trauma may not err by failing to administer additional life-saving hormone. Following prolonged steroid therapy, it is probably wise to cover stressful events during the next six months with parenteral hydrocortisone sodium hemisuccinate.

SUMMARY

A physiological rationale for use of ACTH and synthetic glucocorticoids and mineralocorticoids has been presented.

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CURING CARCINOMA OF THE PROSTATE *

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NEW ORLEANS

That carcinoma of the prostate gland is a major cause of morbidity and mortality is readily apparent. In the Atlanta

* Presented at the Seventy-seventh Annual Meeting of the Louisiana State Medical Society, May 7, 1957, New Orleans.

study, published by the Public Health Service, carcinoma of the prostate ranked first in incidence and prevalence, and third as a cause of death among the major cancers in males. In routine autopsies the incidence has been reported to be as high as 18 per cent.

HORMONAL CONTROL

In the past decade much of the urologic literature has been devoted to the hormonal control of these cancers. There is no doubt about the value of estrogen therapy and castration. Total bilateral adrenalectomy and hypophysectomy have been tried. However, on the basis of our present knowledge and experience, we must state that the endocrine attack on carcinoma of the prostate is strictly palliative and not curative. Even if there are no metastases when estrogens and castration are instituted, over 50 per cent of such patients will be dead within five years.

RADIATION THERAPY

Down through the years radiation therapy in various forms has been tried and discarded. In recent years radioactive gold has been injected into prostatic carcinomas which had extended too far locally to be excised but which had not metastasized distantly. Although some reports on this technique have been encouraging, in our experience it has not cured anyone and has proved quite injurious in a few patients. Experience with supervoltage x-ray in these tumors is too recent to be evaluated, although it is hoped that it is of more value than the other techniques.

At this time we must conclude that the only way of really hoping to cure carcinoma of the prostate is to find the lesion while it is still confined to the prostate and to extirpate it surgically.

DIAGNOSIS

Early detection is possible because about 80 per cent of these cancers begin in the posterior or posterolateral aspects of gland, and therefore, are accessible to palpation on digital rectal examination. Typically these lesions feel considerably harder than normal or hyperplastic prostatic tissue. Approximately 50 per cent of hard nodules of the prostate prove to be carcinomatous on biopsy.

Occasionally, an early occult malignancy is found in tissue removed for relief of bladder neck obstruction due to benign hyperplasia or bladder neck contracture.

In order to feel that a carcinoma of the prostate is potentially curable, there should be no evidence of extraprostatic extension, such as fixation of the gland to surrounding structures, and no elevation of the prostatic fraction of the serum acid phosphatase. There should of course, be no demonstrable distant metastases.

Because so many prostatic nodules prove malignant we feel that if a patient has one, and his general condition and life expectance warrant attempting to cure a possible malignancy, a biopsy should be done if it is not obvious that the hardness is due to something else, such as prostatic calculi, as seen on x-ray, or to tuberculous prostatitis. Although cytologic studies of prostatic secretions, needle biopsies, and transrectal biopsies have been advocated we feel that the best way of obtaining proper biopsy material is by the open perineal route. There is no reason why a hard lump in the prostate should be treated with less respect than a hard nodule in the breast.

SURGERY

The curative surgery in these cases consists of removal of the entire prostate gland, the rim of bladder neck overlying the prostate, the seminal vesicles, the ampullae of the vasa, and most of the anterior layer of Denonvillier's fascia. An anastamosis is then done between the bladder neck and the membranous urethra. This procedure may be done either through the retropubic or perineal approach. We prefer the perineal as the simpler and more direct approach.

Such surgery is usually spoken of as "radical prostatectomy".* Actually, when one thinks of cancer surgery in general, there is nothing radical about it. Even older men tolerate these procedures well as a rule. The operative mortality is low. In the large series reported by Turner and

Belt, it was only 3.9 per cent. In cases we have done at Charity Hospital in New Orleans, there have been no operative deaths. The continuity of the urinary tract is preserved and, although urinary incontinence and fistulae do occur, they are uncommon.

SURVIVAL RATE

Using this total prostatovesiculectomy, the ten year survival rate, in those cases of prostatic carcinoma which are thought to be potentially curable, should be about 50 per cent. It is unfortunate that over the country only about 5 per cent of all carcinomas of the prostate are found early enough to attempt cure. At Charity Hospital in New Orleans, perhaps because of the lack of routine careful physical examination of indigent people, this figure is closer to 1 per cent.

At this time, and using all the tools with which we have to work, our chief hope of raising the dismal overall cure rate in carcinoma of the prostate, is in the more frequent detection of these cancers when they are still early. This must be done by routine, periodic, careful and suspecting palpation of the gland in all men over 40.

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DISCUSSION

Dr. B. E. Trichel (Shreveport): Carcinoma of the prostate, as Dr. Pratt has pointed out, is a common malignancy present clinically in men primarily in the age group 50 years or older. The lesion, by virtue of its origin in 80 per cent of the cases in the posterior lobe of the prostate, localizes itself immediately adjacent to the anterior rectal wall and is easily detectable by digital rectal examination. However, because the lesion is asymptomatic at this stage of its development, only 5 per cent of the cases are diagnosed early enough for radical surgery to be carried out. This fact is regrettable and points out possibly the need for further education of the male public of the advantages to be gained by routine digital rectal examination after age 50, carried out by an experienced examiner.

At the Confederate Memorial Medical Center in Shreveport, we employ the two-stage operation for management of operable carcinoma of the prostate. This technique consists of open exposure of the suspected lesion, using the perineal route. The lesion is identified and liberal biopsy is taken for permanent section. At the same time the posterior surface and lateral margins of the prostate and seminal vesicles are freed from the surrounding tissues. The wound is closed and the patient returned to the ward. Usually in three days a report is rendered by the pathologist. If the diagnosis is carcinoma, then the patient is taken back to the operating room and a radical procedure is carried out, using the retropubic approach.

This mode of management for early carcinoma of the prostate affords the following desirable advantages over other methods of treatment:

1. By open exposure of the prostate, it eliminates the errors of diagnosis inherent in the blind biopsy technique. By providing for a permanent section it further reduces the diagnostic error of frozen tissue technique.

2. It facilitates the technique of surgery by providing the most direct approach to the posterior and anterior surfaces of the gland thereby allowing for the operation to be carried out under direct vision.

3. By performing the operation in two stages, its indication can probably be further extended to include borderline poor risk cases that otherwise would not be candidates for radical surgery.

DUBIN-JOHNSON SYNDROME (CHRONIC IDIOPATHIC JAUNDICE)*

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GUY T. WILLIAMS, M. D.
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NEW ORLEANS

INTRODUCTION

An appraisal of low grade chronic jaundice should encompass a consideration of chronic idiopathic jaundice (Dubin-Johnson syndrome) since it presents features of parenchymal dysfunction and obstruction.

Dubin and Johnson first described this disturbance as chronic intermittent jaun-

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dice occurring principally in young people with vague upper gastrointestinal complaints. Liver profile exhibited features of parenchymal disturbance and obstruction. Cholecystography revealed a nonfunctioning organ. Histological examination of the liver revealed an unidentified pigment arranged radically about the central vein of the hepatic lobule.[1]

REVIEW

Twenty-seven biopsy proven cases have been collected from the literature and are presented in Table 1.

TABLE 1
REVIEW OF REPORTED CASES

Date	Author	No. of Cases
1954	Dubin & Johnson [1]	12
1954	Spring & Nelson [2]	4
1955	Klagman & Efrati [3]	1
1955	Stein [4]	1
1955	Clinicopathological Conference [5] Case Record—Mass. Gen. Hosp.	1
1956	Brown & Schnitka [6]	1
1956	John & Knudtson [7]	2
1956	Nelson [8]	1
1957	McCurley & Muleisen [9]	3
1957	Tamaki & Carfango [10]	1
		27

The frequency is unknown and difficult to establish since some cases were previously reported as infectious hepatitis.[7] Dubin and Johnson reported 12 cases in a review of 4000 liver biopsies.

Jaundice was first detected at birth in one case. The earliest age at which the diagnosis was established was 16 years; whereas the oldest patient was 42 years of age.[1, 9] There were 19 males and 8 females (1 was colored).[5] However, if one excludes the largely military group of Dubin and Johnson, the ratio of males to females is about equal. A familial relationship was suggested in two cases and established in one.[1, 3] The jaundice was intensified by pregnancy and 3 of the 8 females either had spontaneous abortions or delivered deformed fetuses [3, 7, 9] (Table 2).

TABLE 2

Age at which diagnosis established	16-42 years
Age at onset of jaundice	Birth—42 years
Sex—Male	19 cases
Female	8 (1 colored) cases
Family history	2 cases
Number with abnormal births	3 cases

PATHOGENESIS

The nature of the metabolic disturbance concerns: (1) the formation of an iron free, yellowish brown, granular lipogenic, glycogenic, basophilic, fat insoluble, non-bilirubin hemoglobin catabolic pigment, and (2) impaired hepatic parenchymal excretion of (a) the above pigment, (b) gall bladder dye (either oral or intravenous), (c) bromsulphathalein, and (d) bilirubin. The underlying cause remains unexplained.[1, 2, 6, 7]

IDENTIFYING FEATURES

1. Absolute—The criterion "primum" is the histologic demonstration of a coarsely granular, yellowish brown, iron free non-bilirubin pigment, primarily in the hepatic polygonal cells, more heavily concentrated in a "spoke-like" fashion about the central vein of the hepatic lobule, diminishing in intensity toward the periphery. Less frequently, the pigment may be seen in the Kapffer cells [1, 6] (Figures 1 and 2).

2. Presumptive—(1) Clinical: (a) Chronic intermittent jaundice in an otherwise healthy appearing young adult, frequently aggravated by upper respiratory infections, alcoholism, and pregnancy; (b) ill defined upper abdominal discomfort, nausea, anorexia, and rarely fever, (c) slightly enlarged or normal, either tender or

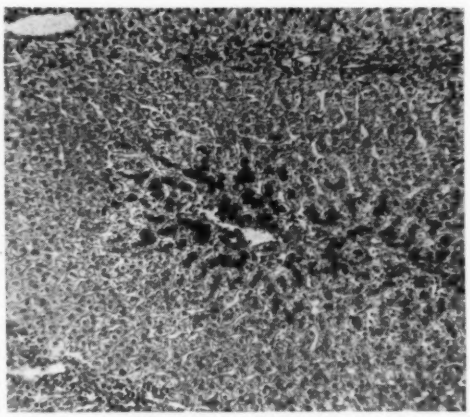

Figure 1.—Pigment in hepatic polygonal cells concentrated in spoke-like fashion about central vein of hepatic lobule.

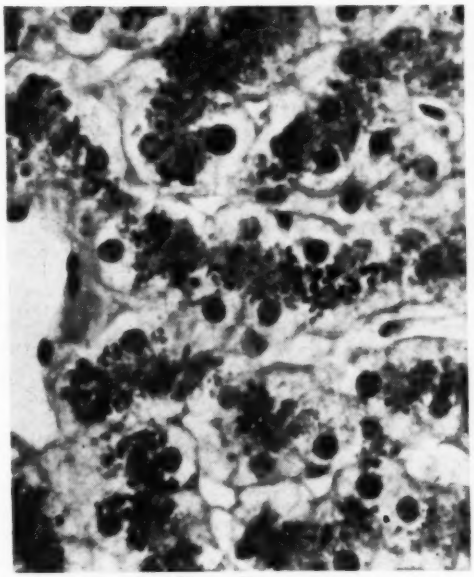

Figure 2.—Kapffer cells.

nontender liver; (d) absence of splenomegaly; (e) frequently dark urine.[1, 6]

3. Laboratory—(a) Normal hemograms, including normal reticulocyte count, osmotic fragility, Coombs' test and normal red cell survival,[1, 9] (b) high frequency of bilirubinuria; (c) elevation of mainly the direct partition of serum bilirubinuria; (d) mildly abnormal parenchymal function tests with BSP retention in the range of 10 per cent, normal total protein and albumin globulin ratio, occasional slight elevations of alkaline phosphatase, cholesterol, cephalin flocculation and thymol; (e) normal fecal urobilinogen and frequently elevated urinary urobilinogen; (f) normal prothrombin time, bleeding and clotting time.[1, 9]

4. Radiographic — Original descriptions reported a nonfunctioning gall bladder. However, since then opacification has been described in 3 cases.[1, 6, 9] Better visualization has been obtained by employing the intravenous technique. Associated gall stones have been reported in 2 instances confirmed in surgery.[6, 7, 9]

Prognosis and longevity are excellent. McCurley and Muleisen reported 1 case (asymptomatic except for jaundice) recently accepted in the air corps.

THERAPY

Because of the benign nature of the disease, no treatment is indicated. Insufficient evidence is available and more cases and experience are necessary before therapeutic abortion can be considered.

DIFFERENTIAL DIAGNOSIS

1. Gilbert's disease (familial nonhemolytic jaundice of physiological hyperbilirubinemia.[11] This inborn type of benign hepatic dysfunction is usually seen in young people and may simulate Dubin-Johnson's syndrome. Gilbert's disease may be identified by: (a) familial history; (b) elevation of indirect bilirubin; (c) absence of bilirubinuria, absence of hepatomegaly and splenomegaly; (d) normal liver function; (e) normal cholecystogram; and (f) normal liver biopsy.

2. Hyperbilirubinemia resulting from residual viral hepatitis may be differentiated by: (a) history; (b) normal cholecystogram; (c) liver biopsy showing either normal liver or evidence of focal necroses, inflammatory reactions and/or portal fibrosis.

3. Hemolytic jaundice may be differentiated by: (a) association of jaundice and evident hemolysis, anemia and reticulocytosis; (b) elevated serum bilirubin principally of the indirect type; (c) increased fecal urobilinogen; (d) frequent splenomegaly; (e) normal liver function tests otherwise; (f) normal cholecystogram; and (g) liver biopsy showing yellowish brown, iron staining, hemosiderin pigment more uniformly distributed throughout the lobule.

4. Obstructive jaundice may be differentiated by: (a) presence of more intense jaundice; (b) diminished or absence of urinary and fecal urobilinogen; (c) normal liver structure with bile plugs and presence of bilirubin pigment in parenchymal cells after prolonged obstruction.

SUMMARY

1. Twenty-seven liver biopsy established cases of Dubin-Johnson's syndrome have been collected from the literature. The authors' experience is concerned with two of these.

2. The absolute criterion for diagnosis

is the demonstration of an iron free, non-bilirubin coarse granular brown pigment in the parenchymal cells about the central vein of the hepatic lobule.

3. The presence of this disease and non-functioning gall bladder does not militate against surgery since cholelithiasis may be associated.

4. Insufficient evidence is available to warrant consideration of therapeutic abortion.

5. Gilbert's disease, residual viral hepatitis, hemolytic jaundice, and obstructive jaundice offer the greatest problem in differential diagnosis.

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NATIONAL DIABETIC WEEK

The yearly cooperative effort by the American Diabetes Association for a week of attention to the finding of hidden diabetics will start on November 17th. This worthy enterprise deserves the help and encouragement of all physicians.

It is thought that one million persons have diabetes who are not aware of it. The American Diabetic Association is the only national group of its type composed exclusively of physicians. Its efforts to improve the care of diabetics and to further their interests are commendable. The success of the total effort depends upon the complementary effort of each physician.

—o—

HOSPITAL FACILITIES COMPARED WITH THE TAX BURDEN IN LOUISIANA

There are too many criteria of comparison in Louisiana in which we are first where we would be better off if we were last.

One of these is the rate of taxation. The state tax handbook issued by the Louisiana Public Affairs Research Council shows that state taxes paid by residents of Louisiana in the fiscal year 1955-1956 were at the rate of $114.94 per capita, or the fifth highest in the nation. But when state taxes are related to per capita income, which reflects the ability of individuals to pay taxes, we have the highest rate in the United States—$8.62 out of every hundred dollars of income per resident.

The tax payers and the legislators will face, as in the past, at the next meeting of the legislature, proposals for expenditure on additional state built, owned, and operated hospitals. In this connection, a timely report in the July 1957 issue of this Journal, by Dougherty, Hitt, and London, entitled "Hospital Facilities in Louisiana, 1953," has presented interesting and important facts concerning the hospital situation in this state. While not purporting to reveal anything new—the facilities are literally under our noses—it displayed figures for a comprehensive look at the hospital picture.

Two points stand out. First, the people of Louisiana have adequate opportunity for hospital care, as compared wlth other southern states and the nation. There are 4.52 general beds per 1000 population, while the average of all the other Southern States is 3.66 beds per 1000 population. The corresponding figure for the nation is 4.19. Louisiana ranks with New York, Pennsylvania, California, Wisconsin, and others in this category of hospital beds.

The second point is (and this is a startling fact) that there are 8,040 private

and 4,804 state general hospital beds in Louisiana. That is, one out of every three general hospital beds in this state is built, owned, and operated by the state with no direct charge made to the occupants using them. This means in terms of costs that for each two days, approximately, of hospital care paid for by the total productive, self sustaining elements of the community in private hospitals, an additional day for indigents must be provided by taxes. Almost half of the babies born in the state each year are born in "free" hospitals. The state is spending almost a million dollars a week on medical care for its people.

When comparisons are made of local and state owned governmental beds of all types, including mental hospitals, Louisiana again outranks the other Southern States and stands a little below the national average. The figures per 1000 population are: United States 5.85, Louisiana 5.17, and the South 4.08.

Our largest State hospital, Charity Hospital of Louisiana at New Orleans, ranks fifth in size, fourth in number of admisions, and first in number of live births.

It is safe to say that one third of the population is not medically indigent. The average medical costs are $67 per person yearly. Louisiana is furnishing a greater quantity of free medical care than other states in the South and in most of the nation. While the health of our people is good, it is not significantly better than that of people in states not spending nearly as much on tax-paid medical care as we are spending.

Experience shows that once any welfare expenditure is established it can never be stopped or even reduced. Every politician elected to an office must advocate the continuance or increase of those "give away" projects already in operation. For this reason, welfare costs in the various forms mount yearly. Taking into account the change in the value of the dollar, and also, the 27 per cent increase in population, the present state administration is spending at a rate two and one half times greater than the rate of the Jones administration in 1940-1944.

Consideration of these facts and figures shows clearly that in general hospital beds, both private and public, the state ranks above the South as a whole, and compares favorably with the rich states of the nation. We are, however, as individuals, carrying the heaviest tax burden in the nation. Accordingly, additional free, tax supported beds should not be built at this time.

ORGANIZATION SECTION

The Executive Committee dedicates this section to the members of the Louisiana State Medical Society, feeling that a proper discussion of salient issues will contribute to the understanding and fortification of our Society.

An informed profession should be a wise one.

SECOND ANNUAL CONFERENCE OF THE COUNCIL ON RURAL HEALTH OF THE AMERICAN MEDICAL ASSOCIATION HELD AT PURDUE UNIVERSITY, LAFAYETTE, INDIANA, FOR THE CHAIRMEN AND MEMBERS OF THE STATE RURAL HEALTH COMMITTEES

This year's session, again headed by Dr. F. S. Crockett in his home town, was attended by about forty-five members, including the Executive Secretary of some of the state committees. It was a one and one-half day meeting that started Friday morning, October 4, 1957, at 9:00 A.M. and finished at 12:00 Noon, Saturday, October 5, 1957.

The first morning's session was given over to discussion by Dr. George Beal and Dr. Joseph Bolin, Sociologists at Iowa State College, on "How Rural People Accept New Ideas". This program demonstrated how new ideas were suggested to two or three "key people" and demonstrated the technique used by which the problem was finally carried out, the goal reached, and the plan accomplished.

The afternoon of Friday was given over to three speakers. Mr. C. A. Vines, Secretary, Extension Committee on Organization and Policy, Land Grant College Association, Little Rock, Arkansas, Mr. Beatty H. Demit, Chairman, National Grange Interim Health Committee, Indiana, Pennsylvania, and Mr. Charles B. Shuman, President, American Farm Bureau Federation, Chicago, Illinois. These speakers gave their own ideas on public health and what the three organizations were doing to accomplish better rural health and the utilization of all the facilities at hand for the consummation of this problem.

Mr. Vines brought out adequately the role of the County Agent in stimulating good medical care in his community. Mr. Demit went into detail in reference to some of the plans the National Grange had worked out in connection with the interest of the health of its community. Mr. Shuman explained the stand of the American Farm Bureau in better medical care, and all three insisted that their own organizations were strongly against socialized medicine as is the medical profession.

A social hour was enjoyed in the home of Dr. F. S. Crockett and a banquet that night at Purdue University's Union Building was well attended. The speaker at the banquet was Dr. Earl Butz, Dean of Agriculture and Director, Agricultural Extension Service, Purdue University, Lafayette, Indiana, and a former assistant to Mr. Benson in Washington, D. C. The title of his discussion was "Big Government and You." It was very enlightening to hear a man of Dr. Butz's experience, who had spent two years in government service, explain the many difficulties in over-regimentation. In spite of the many reasons he gave for big government, big spending, and big ideas of the bureaucrats, he was unable to give us specific answers. He chided us for some of our complacency, but warned us to be ever alert and to keep in constant contact with our senators and representatives.

Saturday morning was given over to discussion of the individual problems of the Chairmen and Secretaries of the different states. Some excellent reports were brought out from North Carolina, Ohio, Pennsylvania, and California.

It is the studied judgment of your chairman that Louisiana, with its State Health Council and the local Health Councils, probably still leads the country, for the most part, in its many accomplishments.

We promised the group that Louisiana would try to help Mississippi entertain the Thirteenth Health Conference next March 6-8, at Jackson, Mississippi.

J. P. Sanders, M. D.
Chairman
Rural and Urban Health Committee

FINAL STATUS OF MEDICAL LEGISLATION AT ADJOURNMENT OF THE FIRST SESSION 85TH CONGRESS

The following material has been furnished us by the Washington office of the American Medical Association:

This is an interim report on health and medical legislation in the 85th Congress. It summarizes all action taken on health measures up to the time of adjournment on August 30, and lists all bills that will be awaiting decision in the second session starting January 7, 1958.

The small number of health-medical bills enacted this year might be regarded as deceptive. Actually 441 of these bills were introduced—a record total even for a first session. Congress deferred action on most of them for a variety of reasons—a desire for more extensive hearings, economy, and, possibly, an inclination to save popular-appeal bills for next year. Experience has shown that the second session, always an election year, is the crucial one, when forces line up for final decisions on the big, controversial medical bills.

For example, no action was taken this year on such important measures as U. S. aid to medical schools and health insurance for federal civilian workers, nor on a growing list of ideas for government-paid hospitalization of OASI beneficiaries, a proposal that would have an obvious impact on the practice of medicine. There is every reason to believe Congress will not neglect these subjects next year.

HEALTH LEGISLATION ENACTED

Doctor Draft Extension (P.L. 85-62)—Because the doctor draft was set to expire July 1, this was one of the first health measures passed by the 85th Congress. It gives Selective Service authority until July 1, 1959 (when both this amendment and the regular draft expire) to call certain physicians up to age 35 for military service. Only those under age 35 with obligations under the regular draft and who have been deferred for any reason may be called. Defense Department, meanwhile, says it is getting enough medical school graduates as reservists to preclude use of the new law at this time.

Medical Research (P.L. 85-67)—Another early enactment was the fiscal 1958 budget for the

Department of Health, Education, and Welfare. Congress voted $2,503,130,381 for all HEW programs, including record high totals for medical research through the National Institutes of Health. Congress can—and in all likelihood will—receive requests from the Administration for additional money during the current fiscal year through a deficiency appropriation.

Vendor Medical Payments (P.L. 85-110)—This law is intended to resolve some problems arising out of the Social Security Amendments of 1956 with particular reference to vendor medical payments for public assistance recipients. Under P.L. 110, states are given the choice of either: (a) using federal funds for vendor medical payments within the $60 a month per recipient maximum; or (b) establish a single medical vendor payment financed by federal funds which were set by a 1956 law at one-half of $6 a month per adult and one-half of $3 per child, to be matched by states. States also can continue to make direct payments to recipients for medical and subsistence expenses.

Disability Freeze Extension (P.L. 85-109)—Under this law, a new deadline of July 1, 1958, is established for disabled persons covered under social security to apply for full retroactivity under the disability freeze passed in 1954. Applications filed by next July will allow workers to count the full period of disability provided they were eligible at the time the disability was incurred. After next July 1, any period of disability established for a worker cannot begin earlier than one year before the application is filed.

Indian & Non-Indian Hospitals (P.L. 85-151)—At the urging of some western members of Congress, P.L. 151 was enacted to authorize federal funds to help build non-profit or public hospitals and diagnostic or treatment centers on or near Indian reservations; the extent of federal contribution will be determined by the percentage of care given eligible Indians. Facilities have to agree to care for Indians and non-Indians.

Vocational Rehab. Traineeships (P.L. 85-198)—This measure extends from two to three years the maximum period of time over which the federal government can pay for partial financing of traineeships in physical medicine and rehabilitation. It amends the Vocational Rehabilitation Act which was expanded in the 83rd Congress.

Vocational Rehab. Planning (P.L. 85-213)—This amends the Vocational Rehabilitation Act by extending the time federal funds may be used for planning, preparing and initiating expansion of programs in the states. Congress was asked to act when the July 1 deadline approached with considerable unexpended funds on hand.

Codification of Veterans Laws (P.L. 85-56)—Without making any substantive changes in existing law, this Congress brought into a single code all veterans benefit laws, including those providing for hospital and medical care. Some laws date back thirty years.

Poultry Inspection (P.L. 85-172)—Under this law, federal inspection of poultry moved in interstate commerce becomes compulsory.

Military Nurses Incentives (P.L. 85-155)—In line with earlier efforts to make careers in the military more attractive, Congress passed this law improving career prospects for military nurses by making more and higher ranks available.

BILLS THAT PASSED ONE BRANCH OF CONGRESS

Pulmonary Tuberculosis (H.R. 1264)—The bill, declaring veterans suffering from active pulmonary tuberculosis to be permanently and totally disabled for pension purposes while hospitalized, passed the House but is pending in the Senate Finance Committee.

HEARINGS HELD BUT NO FURTHER ACTION TAKEN

Bricker Amendment (S.J. Res. 3)—The long-standing proposed amendment to the Constitution by Senator Bricker (R., Ohio) limiting the domestic effect of treaties and other international agreements.

Civil Aviation Medicine (S. 1045)—Would establish in the Civil Aeronautics Administration an Office of Civil Aviation Medicine along with a Medical Research Institute.

Welfare-Pension Plans Registration (S. 1122, S. 2888)—Provide for registration, reporting and disclosure of employee welfare and pension benefit plans. Both House and Senate Committee hearings held and some action expected next session.

Highway Safety (S. 1292)—Hearings in House but not on any specific bills. Proposals include compulsory installation of safety belts.

OVR Pilot Center (S. 2068)—Would give the Office of Vocational Rehabilitation authority to use federal funds for construction of facilities for a pilot rehabilitation center in the Washington, D. C., area.

Non-Service-Connected Care (H.R. 58)—Would impose added requirements on veterans with non-service-connected disabilities seeking hospitalization or domiciliary care in VA facilities.

Barbiturates and Amphetamines Control (H.R. 503 & others)—Regulate the manufacture, distribution and possession of habit-forming barbiturate and amphetamine drugs, and provides for registration and record-keeping, but with doctors exempted.

Department of Civil Defense (H.R. 2125 & others)—Establish a new executive Department of Civil Defense which would have supremacy over the military in times of disaster in certain defense areas.

Salary Rise for VA Doctors (H.R. 6719)—Increases salaries of medical personnel in VA, and also raises optometrists to the level of physicians. (Reported in House.)

Chemical Additives (H.R. 6747 & others)—Requires pre-testing of many chemical additives to be used in food processing and marketing. The House has held extensive hearings on this subject.

Grants-in-Aid Study (H. Res. 312)—Provides for a Select Committee of the House to study federal grants-in-aid to state and local governments, and other groups. It got as far as House Rules Committee approval.

Advisory Committee for the Blind (H.R. 8427)—Establishes a temporary Presidential commission to study and report on the problems relating to blindness and the needs of blind persons.

BILLS STILL IN COMMITTEE; NO HEARINGS HELD

Hospitalization for Aged (H.R. 9467, 9448 & others)—Various bills provide through different approaches a certain number of days of free hospitalization each year for Old-Age and Survivors Insurance recipients and beneficiaries; some bills also would pay in-hospital surgical and medical care costs.

Compulsory Health Insurance (S. 844, H.R. 3764)—A 1957 version of the old and rejected national compulsory health insurance measures of 1948, the sponsors being Senator Murray (D., Mont.) and Rep. Dingell (D., Mich.).

Liberalizing OASI Coverage (S. 173 &-others)—These measures would liberalize age and coverage requirements in the OASI disability program.

OASI Coverage for Doctors (H.R. 8883)—Physicians would be brought under Social Security on a compulsory basis.

Jenkins-Keogh Plan (H.R. 9 and 10)—Defer federal income taxes on portions of earnings of the self-employed for the purchase of retirement plans.

OASI Wage Base Increase (H.R. 7669)—Increases the wage base, on which tax is computed, from the present $4,200 to $6,000.

Federal Workers Health Insurance (S. 2339 & others)—Provides for a voluntary, contributory health insurance program for federal civilian employees and their dependents; both basic and major medical coverage included.

Overseas Federal Medical Care (H.R. 6141)—Provides health and medical services for U. S. civilians overseas who are employed in government jobs, and also would cover their dependents.

Federal Medical School Aid (H.R. 6874)—Authorizes federal grants to medical schools and research facilities for construction of classrooms and laboratories for teaching.

National Radiation Institute (S. 1228 & H.R. 4820)—Establish a National Radiation Health Institute within the National Institutes of Health.

Lobbying Act Amendments (S. 2191, H.R. 8346)—Would rewrite regulations covering lobbyists and lobbying in Congress.

Federal Loans to Hospitals (H.R. 1979)—For those hospitals interested in construction loans rather than Hill-Burton grants, these bills would authorize long-term government loans.

Reinsurance (S. 1750, H.R. 6506)—Permits pooling by various insurance companies without regard to the antitrust laws for purpose of encouraging new experiments in health insurance coverage.

Aid for the Aged (H.R. 383 and others)—Authorizes grants for studies and projects for the aged.

Federal Advisory Health Council (H.R. 2435 & others)—Establishes a Federal Advisory Council on Health, as recommended by the Hoover Commission.

Longshoremen's Act (H.R. 7303, S. 2400)—Amends Longshoremen's and Harbor Workers' Compensation Act so that injured workers can select their own physician and hospital.

Labeling for Household Use (H.R. 7388 & others) — Regulating the labeling of hazardous substances intended for household use.

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MEDICAL NEWS SECTION

CALENDAR

PARISH AND DISTRICT MEDICAL SOCIETY MEETINGS

Society	Date	Place
Calcasieu	Fourth Tuesday every other month	Lake Charles
East Baton Rouge	Second Tuesday of every month	Baton Rouge
Morehouse	Third Tuesday of every month	Bastrop
Natchitoches	Second Tuesday of every month	
Orleans	Second Monday of every month	New Orleans
Ouachita	First Thursday of every month	Monroe
Rapides	First Monday of every month	Alexandria
Sabine	First Wednesday of every month	
Tangipahoa	Second and fourth Thursdays of every month	Indepencence
Second District	Third Thursday of every month	
Shreveport	First Tuesday of every month	Shreveport
Vernon	First Thursday of every month	

THE MEDICAL DEPARTMENT UNITED STATES ARMY IN WORLD WAR II

Surgery in World War II, Ophthalmology and Otolaryngology

In time of war the specialties of ophthalmology and otolaryngology must treat the diseases and meet the demands of what amounts to a tremendous civilian practice, while at the same time treating devastating combat-incurred injuries of these specialized areas. Intraocular foreign bodies are a serious peacetime industrial problem. In wartime, the management of these injuries is a heavy burden quantitatively. The destructive effects of wounding agents make them a far heavier burden qualitatively.

Introductory chapters in both sections of this volume deal with the administrative aspects of wartime ophthalmology and otolaryngology.

Part I describes the major ophthalmologic conditions, both traumatic and non-traumatic, encountered in World War II. Eye centers for the treatment of these injuries with concentrated, specialized care, were established overseas and in the United States. Eyes which might otherwise have been lost were conserved. These centers carried out their missions with a notable economy of personnel and equipment. Also described is the artificial eye program, a brilliant example of Medical and Dental Service cooperation in a new technique.

Part II covers the major problems of otolaryngology in wartime as seen by the general medical officer as well as by the highly trained specialist. There is a section on narcosynthesis.

There are detailed accounts of the Army programs for rehabilitation of the blinded and the deafened casualties. The lessons learned, the objectives attained, are directly applicable to any peacetime management of the blind and the deaf.

Copies may be obtained from Superintendent of Documents, Government Printing Office, Washington 25, D. C.—$5.00 per copy. (Catalog No. D 104.11:Su 7/7).

The following volumes are also available:

Hospitalization and Evacuation, Zone of Interior, World War II. 1956. 503 p. il.
Cloth, **$4.00** Catalog No. D 114.7:M 46/v.1

Dental Service in World War II. 1955. 362 p. il.
Cloth, **$3.25** Catalog No. D 104.11:D 43

Preventive Medicine in World War II, Volume II, Environmental Hygiene. 1955. 404 p. il.
Cloth, **$3.50** Catalog No. D 104.11:P 92/v.2

Preventive Medicine in World War II, Volume III, Personal Health Measures and Immunization. 1955. 394 p. il.
Cloth, **$3.25** Catalog No. D 104.11:P 92/v.3

Surgery in World War II, Hand Surgery. 1955. 447 p. il.
Cloth, **$3.75** Catalog No. D. 104.11:Su 7/2

Surgery in World War II, General Surgery. 1955. 417 p. il.
Cloth, **$4.25** Catalog No. D 104.11:Su 7/4/v.2

Surgery in World War II, Physiologic Effects of Wounds. 1952. 376 p. il.
Cloth, **$3.50** Catalog No. D 104.11:Su 7

Surgery in World War II, Vascular Surgery. 1955. 465 p. il.
Cloth, **$4.25** Catalog No. D 104.11:Su 7/3

Surgery in World War II, Ophthalmology and Otolaryngology. 1957. 632 p. il.
Cloth, **$5.00** Catalog No. 104.11:Su 7/7

Orthopedic Surgery in the European Theater of Operations. 1956. 397 p. il.
Cloth, **$4.00** Catalog No. D 104.11:Su 7/5

Orthopedic Surgery in the Mediterranean Theater of Operations. 1957. 368 p. il.
Cloth, **$4.00** Catalog No. D 104.11:Su 7/6

THE NEW ORLEANS GRADUATE MEDICAL ASSEMBLY

The twenty-first annual meeting of The New Orleans Graduate Medical Assembly will be held March 3, 4, 5 and 6, 1958, headquarters at the Roosevelt Hotel.

Eighteen outstanding guest speakers will participate and their presentations will be of interest to both specialists and general practitioners. The program will include fifty-four informative discussions on many topics of current medical interest, in addition to clinicopathologic conferences, symposia, medical motion pictures, round-table luncheons and technical exhibits.

The Assembly has been officially approved for Category I by the Commission on Education of the American Academy of General Practice. Thirty hours of formal credit will be allowed for attendance at this meeting.

Following the meeting in New Orleans, arrangements have been made for a postclinical tour to Mexico City, Cuernavaca, Taxco and Acapulco, leaving from New Orleans on Friday, March 7 and returning on Tuesday, March 18.

Details of the New Orleans meeting and the postclinical tour are available at the office of the Assembly, Room 103, 1430 Tulane Avenue, New Orleans 12, Louisiana.

LOUISIANA ACADEMY OF GENERAL PRACTICE

The Eleventh Annual Assembly of the Louisiana Academy of General Practice was held October 8-10, 1957, at Monroe, Louisiana. Dr. Julius Daigle, Paincourtville, Louisiana is president of the Academy. Speakers on the scientific program included:

Dr. R. L. Sanders, Memphis, Tenn.
Dr. T. B. Moore, Memphis, Tenn.
Dr. E. S. McLarty, Galveston, Texas
Dr. W. E. Guerriero, Dallas, Texas
Dr. H. E. Banghart, Philadelphia, Pa.
Dr. D. L. Anderson· Monroe, Louisiana

The luncheon meeting on October 9, was addressed by Dr. J. P. Culpepper, Hattiesburg, Miss., President of the Southern Medical Association.

Featured speaker at the Annual Banquet was Dr. H. T. Jackson, Fort Worth, Texas, President-elect of the American Academy of General Practice.

THE NEW ORLEANS GRADUATE MEDICAL ASSEMBLY

The twenty-first annual meeting of the New Orleans Graduate Medical Assembly will be held March 3-6, 1958, headquarters at the Roosevelt Hotel. Listed below are the Chairmen and Vice-chairmen of the Program Committees for this year:

CARDIOLOGY AND INTERNAL MEDICINE
Philip H. Jones, M. D., Chairman
George E. Burch, M. D., Vice-chairman

DERMATOLOGY
Lee D. McLean, M. D., Chairman
V. Medd Henington, M. D.,Vice-chairman

GASTROENTEROLOGY
Donovan C. Browne, M. D., Chairman
Daniel N. Silverman, M. D., Vice-chairman

GENERAL PRACTICE
Mannie D. Paine, Jr., M. D., Chairman
Nicholas J. Chetta, M. D., Vice-chairman

GYNECOLOGY
C. Gordon Johnson, M. D., Chairman
Curtis Tyrone, M. D., Vice-chairman

NEUROPSYCHIATRY
Theodore L. L. Soniat, M. D., Chairman
T. A. Watters, M. D., Vice-chairman

OBSTETRICS
Fred K. Vaughn, M. D., Chairman
Isadore Dyer, M. D., Vice-chairman

OPHTHALMOLOGY
William B. Clark, M. D., Chairman
George M. Haik, M. D., Vice-chairman

ORTHOPEDIC SURGERY
Lyon K. Loomis, M. D., Chairman
Rufus H. Alldredge, M. D., Vice-chairman

OTOLARYNGOLOGY
Lucian W. Alexander, M. D., Chairman
Charles L. Cox, M. D., Vice-chairman

PATHOLOGY
Edwin H. Lawson, M. D., Chairman
Andrew V. Friedrichs, M. D., Vice-chairman

PEDIATRICS
W. C. Rivenbark, M. D., Chairman
James E. Bailey, M. D., Vice-chairman

RADIOLOGY
Meyer D. Teitelbaum, M. D., Chairman
William S. Neal, M. D., Vice-chairman

SURGERY
Howard Mahorner, M. D., Chairman
Ambrose H. Storck, M. D., Vice-chairman

UROLOGY
W. E. Kittredge, M. D., Chairman
Max M. Green, M. D., Vice-chairman

LIVER AILMENT GROWS AS PUBLIC HEALTH PROBLEM

Infectious hepatitis, a liver ailment, is creating more interest among public health workers than probably any other virus disease except polio, an American Medical Association publication said recently.

The number of reported cases has "jumped dramatically" since hepatitis was added to the list of nationally reported diseases in 1952, and it is now the third most common infectious disease in the U. S., according to an article in February Today's Health.

"Whether this represents an actual increase in incidence or merely better recognition . . . is open

to question. But one thing is certain: never before has concern over it been so high," Miss Marion A. Briggs, a New York free lance writer, said in the article.

Its importance is not in the number of deaths it causes, which are few (only three to five in 1,000 cases), but in the long time its victims must spend in convalescence—from two to three months.

In addition, it is estimated that about 30 per cent of the adult population has had infectious hepatitis without knowing it. These mild unrecognized cases constitute a threat to a community since they provide unknown carriers of the disease, Miss Briggs said.

Infectious hepatitis, called "camp jaundice," "field jaundice," "catarrhal jaundice" and "infectious jaundice" in the past, is an inflammation of the liver; one of its common symptoms is jaundice—a yellowish color of the skin and eyes.

A major problem created by the disease is that its causative agent—generally believed to be a virus—has never been isolated. This in turn has prevented the development of a specific treatment or a preventive vaccine. The best treatment is still bed rest and a good diet.

Hepatitis' most common means of spreading is apparently by personal contact. When one member of a family gets it, other members almost always get it too. It has been known to be spread by drinking water, food, and milk. Flies have also been suspected.

TESTS SHOW CHEWING TOBACCO'S EFFECT ON BODY

Heart researchers provided some new information for doctors wishing to advise their patients about the effects of chewing tobacco on the circulatory system.

Although 81 million pounds of chewing tobacco are consumed annually in the U. S., practically nothing is known about its effect on the body. However, four Cincinnati researchers now have conducted a series of tests on men who habitually chewed tobacco. They reported their findings in the Feb. 2 Journal of the American Medical Association.

They found that chewing tobacco produced changes in the body similar to those caused by smoking cigarettes, including increases in pulse rate and blood pressure and a decrease in skin temperature. It also produced changes in the ballistocardiograph, which measures the impact on the body of the heart's thrust as it pumps blood. Smoking did not produce ballistocardiograph changes.

The 24 men, ranging in age from 34 to 71 years, chewed low-nicotine tobacco or a regular commercial brand. Some also chewed gum for comparison.

After chewing commercial tobacco, the pulse rates of 14 men increased markedly, with a average increase of 13.4 beats a minute. With low-nicotine tobacco, the rate remained constant in three men, decreased in one and increased by an average of 6.5 beats a minute in nine men. After chewing gum one man showed a slight rise and one a slight fall.

All showed definite increases in blood pressure after chewing commercial tobacco.

In most of the men the pattern of skin temperature changes was similar to that reported in cigarette smoking studies. Forehead temperatures remained nearly constant with both types of tobacco and gum, but temperatures in the fingers and toes decreased after chewing tobacco.

The ballistocardiograph changes, which were recorded in 23 men, were the greatest about 14 minutes after chewing began. Younger men who smoked in other studies did not show such changes.

The possibility that more nicotine is absorbed by the body during chewing than during smoking might explain these changes in the older men, the authors said.

The average amount of tobacco chewed contained about 10 times more tobacco than the standard cigarette. In addition, the tobacco was held in the mouth longer than cigarette smoke usually is. It is estimated that more than two-thirds of the nicotine in cigarette smoke is absorbed through the membranes of the mouth.

Conducting the research, which was supported by a grant from the Tobacco Industry Research Committee, New York, were Dr. David L. Simon, Dr. Arnold Iglauer, Dr. John Braunstein and Robert E. Rakel of Cincinnati General Hospital and Kettering Laboratory, University of Cincinnati.

TUBERCULOSIS

Veterans administration hospitals are safe places for volunteers to work, so far as danger of getting tuberculosis goes. Although tuberculosis afflicts about one out of every 1,000 persons in the general population, a survey of VA hospitals and other installations showed not one of 11,375 volunteer workers developed the disease after coming on duty. News Item, Sc. News Letter, Nov. 3, 1956.

It is generally accepted that tuberculosis is the most common cause of pulmonary cavitation. That tuberculosis is a frequent occurrence in third-stage silicosis is evident when one considers that over 50% of the conglomerate masses are said to be infected with tuberculosis. Thus, when cavitation occurs in a conglomerate mass, it is usually presumed to be of tuberculosis nature. However, the occurrence of nontuberculous cavitation must not be overlooked. C. S. Morrow, M.B. and R. N. Armen, M.D., Annals of Internal Med., Oct. 1956.

It has never been possible to confine a disease such as tuberculosis to a narrow specialty. G. L.

Wherrett, M.D., Canadian J. of Pub. H., Nov. 1956.

True progress in law, in medicine—in almost any area of vital human concern—will come from the discovery and cultivation of common interests by people who share a common purpose, unadulterated by special political objectives or ideological differences. Editorial, World Med. J., May, 1956.

All diabetics should have annual chest X-rays. Any sudden increase in insulin requirements or loss of weight, even though it appears voluntary, should be followed by a roentgenographic examination of the chest. By earlier diagnosis the prognosis of tuberculosis in the diabetic will be immeasurably improved. Treatment of both diseases must be aggressive. Robert H. Joelson, M.D., Henry Dolger, M.D., J. of Mt. Sinai Hosp. of N. Y., July-Aug. 1956.

Until recently the emphasis of tuberculosis control programs has been centered on mass surveys, mobile roentgenographic units, and hospital admissions, while a segment of the population with one of the highest rates of infection has been somewhat neglected. Continuous case-finding programs in prisons offer a fertile field for the control of tuberculosis for several reasons. The increased prevalence rate of the disease in prisoners make such programs much more rewarding than are those which are carried out in the general population. Harvey I. Meyers, M.D., George Jacobson, M.D., and Frank W. Oechsli, M.D., Am. Rev. of Tuberc., Oct. 1956.

WOMAN'S AUXILIARY TO THE LOUISIANA STATE MEDICAL SOCIETY

WOMAN'S AUXILIARY LOUISIANA STATE MEDICAL SOCIETY ORLEANS PARISH

The Woman's Auxiliary to the Orleans Parish Medical Society held its first meeting of the fall season Wednesday afternoon October 9th at the Orleans Club. The president Mrs. Eugene H. Countiss presided.

Mrs. Boni J. DeLaureal, president of the Woman's Auxiliary to the Louisiana State Medical Society, was guest of honor at the tea and program which followed the meeting. Mrs. DeLaureal spoke on "The Doctor's wife in volunteer work in the community". It inspired us all to want to 'dig in' and accumulate a great number of hours of work in cancer, American Heart, Red Cross, hospital auxiliary work and the many other branches of volunteer services.

Of interest to the mothers, grandmothers and "aunts" was the program given by Mmes. John Guarisco and Charles Giblin who spoke on "The Child in the Nursery School".

Receiving with Mrs. Eugene H. Countiss were Mesdames Boni J. DeLaureal, Albert F. W. Habeeb and Mrs. Abe Golden.

Hostesses for the afternoon were Mesdames James L. Treadway, Albert B. Pavy, Jr., Daniel W. Beacham, Charles Farris, Jr., Carl Gulotta, B. Holly Grimm and William S. Neal. Mrs. Fred O. Brumfield is chairman of hostesses.

The tea table was centered with a beautiful arrangement of flowers in the autumn shades and presiding at the silver coffee and tea services were Mesdames Walter F. Becker and Frank S. Oser, Jr.

Mrs. Branch J. Aymond,
Publicity Chairman.

BOOK REVIEWS

Etiologic Factors in Renal Lithiasis; by Arthur J. Butt, Springfield, Illinois, Charles C Thomas, 1956, Pp 401. Price $12.50.

The author with nineteen contributors discusses the various factors and hypotheses in renal lithiasis. The complex picture is presented in eighteen chapters, and the topics range from anatomy to urinary calculi analysis.

The subject matter is well organized and the coverage in each chapter is comprehensive. An attempt is made to correlate past with present findings and the presentation of divergent views on the etiology of renal lithiasis enables the reader to obtain a balanced perspective. In his foreword, W. F. Braasch considers that the book obtains an intelligent appraisal of advances made in the etiology of urinary calculi.

The extensive bibliography and the wide coverage of the various types of calculi make the book a valuable source of reference. Of particular interest is the development of the role colloids and ground substance play in stone formation. The use of hyaluronidase by the author in stone prevention is thought-provoking. He emphasizes that it is merely an adjunct in stone therapy and that the dosage must be controlled from day to day otherwise the drug may prove harmful.

The book should prove helpful to urologists, in-

ternists, surgeons, endocrinologists, chemists, and research workers.

JOHN G. MENVILLE, M. D.

Roentgen Signs in Clinical Diagnosis; by Isadore Meschan, M. A., M. D., with the Assistance of R. M. F. Farrer-Meschan, M. B., B. S., (Melbourne, Australia). Philadelphia and London, W. B. Saunders Co., 1956, Pp. 1058, illus., 2216 on 890 figures, Price, $20.00.

While it was the intention of the authors that this volume could be employed independently of their previous work, "Atlas of Normal Radiographic Anatomy" and is a separate didactic presentation, the two volumes result in an excellent and most satisfying combination of informative material covering normal anatomy and the roentgen signs of disease processes. The author's approach to the teaching of radiology is intended to furnish: "an objective description of the aberration from the normal"; and, "an integration with the known clinical data to arrive at an impression or differential diagnosis".

There are thirty-one chapters and an index. The first three chapters are devoted to fundamental principles, protection from roentgen irradiation and the functions of the radiologist. Chapters Four through Eleven are concerned with the normal and abnormal roentgenology of bones and joints. Fractures, congenital abnormalities and bone disease are comprehensively covered. The organization of bone diseases into radiolucent lesions involving multiple bones and a single extremity as distinguished from osteosclerotic and hypertrophic bone diseases of the extremities is noteworthy and immeasureably increases the reference value of this text.

The skull and facial bones are discussed in Chapters 12 and 13. The division of the lesions of the skull bones into single and multiple, diffuse and demarcated, radiolucent and increased radiopacity is a valuable contribution. Chapter 14 is concerned with the radiography of the vertebral column.

Chapters 15 through 23 consider the chest and its subdivisions. These sections are also organized into the single and multiple, diffuse and nodular, regular and irregular pneumonic lesions. Chapter 19 considers those pulmonary lesions characterized by increase in linear markings. The lung lesions characterized by increased radiolucency in the lung fields is covered in Chapter 20.

Chapter 24 is devoted to the value of the plain survey of the abdomen. The radiography of the urinary tract and suprarenal glands is covered in Chapter 25. The gall bladder and its functions and diseases are discussed in Chapter 26.

The gastro-intestinal tract is comprehensively covered in Chapters 27 through 30. Chapter 31 is concerned with radiography in obstetrics and gynecology.

The index is adequate and the references are intentionally limited to provide the reader with "key" articles which will provide additional references. The diagrams and illustrations are outstanding and numerous. The legends are adequate and clear. The text is well-written, comprehensive and interesting. This text and the "Atlas of Normal Radiographic Anatomy" are valuable contributions to every physician interested in diagnostic roentgenology.

J. N. ANÉ, M. D.

PUBLICATIONS RECEIVED

Dover Publications, Inc., N. Y.: Fads and Fallacies in the Name of Science, by Martin Gardner (formerly published under the title In the Name of Science).

Grune & Stratton, N. Y.: A Mount Sinai Hospital Monograph on The Malabsorption Syndrome, edited by David Adlersberg, M. D.; Roots of Modern Psychiatry, by Mark D. Altschule, M. D., with the collaboration of Evelyn Russ; General Techniques of Hypnotism, by Andre M. Weitzenhoffer, Ph.D.

Paul B. Hoeber, Inc., N. Y.: Clinical Gastroenterology, by Eddy D. Palmer, M. D.; Introduction to Biostatistics, by Huldah Bancroft, Ph.D.

The C. V. Mosby Co., St. Louis: Headache, Diagnosis and Treatment, by Robert E. Ryan, M. D. (2nd edit.)

Philosophical Library, N. Y.: Manual of Nutrition; The Chronically Ill, by Joseph Fox, M. D.

W. B. Saunders Co., Phila.: The Story of Peptic Ulcer, conceived by Richard D. Tonkin, M. D., and characterized by Raymond Keith Hellier, F.R.S.A.

Charles C Thomas, Publisher, Springfield, Ill.: Methods in Surgical Pathology, by Henry A. Teloh, M. D.; The Dermatologist's Handbook, by Ashton L. Welsh, M. D.; The Infantile Cerebral Palsies, by Mrs. Eirene Collis, Dr. W. R. F. Collis, Dr. William Dunham, Dr. L. T. Hilliard, Dr. David Lawson, and Sir Francis Walshe; Technique of Fluid Balance, Principles and Management of Water and Electrolyte Therapy, by Geoffrey H. Tovey, M. D.; The Bases of Treatment, by Neuton S. Stern, M. D., and Thomas N. Stern, M. D.; Diseases of the External Ear, by Ben H. Senturia, M. D.

Williams & Wilkins Co., Baltimore: Extensile Exposure, by Arnold K. Henry, M. D. (2nd edit.)